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FACTS ON FLUORIDATION

CANADIAN DENTAL ASSOCIATION
234 ST. GEORGE STREET
TORONTO, CANADA

Revised July, 1957

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Canadian Dental Association. Research Committee

FACTS
ON
FLUORIDATION

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FACTS ON FLUORIDATION

I. NATURAL OCCURRENCE OF FLUORINE* IN FOOD AND WATER

Most natural water supplies and many different foods contain trace quantities of fluorine. Thus, under normal conditions of living, minute quantities of fluorine are consumed in the daily diet.

The widespread occurrence of fluorine in food is shown in Table I, (page 26). Approximately 0.2 - 0.3 milligrams of fluorine are ingested daily in the food we eat (Armstrong, 1943). The amount of this fluoride absorbed is too small to have any detectable effect on the body. Only certain teas, fish and bone meal preparations contain quantities of fluoride that may be of significance in nutrition. The most significant intake of fluoride is through the medium of drinking water. The amount of water consumed by adults in temperate climates is about 1200 to 1600 cc. daily (McClure, 1943). If water contains 1.0 p.p.m. (parts per million) of fluorine, approximately 1.2 - 1.6 mg. of fluorine is consumed daily. It is evident that water containing fluorine is the major source of this trace element.

Populations in many parts of the world such as Argentina, Canada, China, England, India, Italy and the United States have for centuries been drinking water in which fluoride occurs naturally. In the United States more than 4,000,000 people have used water containing fluoride in a concentration of 3.1 -5.0 p.p.m. for several generations. A chart locating some of the natural fluoride-bearing water supplies in Canada is appended as Appendix I and will be found on page 34.

*Fluorine is one of the most active elements of the halogen family. On account of its affinity for other elements it is seldom found free in nature. When combined with other elements to form a salt it is called a fluoride, for example, sodium fluoride.

II. ENDEMIC DENTAL FLUOROSIS (MOTTLED TEETH)

The finding that there is a relation between fluorine and dental health had its beginning in the discovery, in 1931, that high fluoride concentrations in water cause a condition known as endemic dental fluorosis (mottled teeth). This condition is due to a disturbance in the calcification of enamel and dentin and in its mildest form produces a chalky white enamel surface. As the fluoride concentration increases (4 - 8 ppm), discrete or confluent pitting of the enamel surface with brown staining may occur. The severity of dental fluorosis is proportional to the concentration of fluoride in the drinking water that is consumed during that period in childhood when the teeth are being formed. Endemic dental fluorosis in a readily observable form appears only when the fluoride supply in the water exceeds 2.0 p.p.m. (Deatherage, 1941).

It was observed among children using fluoride-bearing water that the incidence of dental caries was very low, whether or not their teeth showed signs of fluorosis. This observation led to extensive epidemiological studies dealing with the relationship between fluoride and dental caries.

III. RELATION OF FLUORIDES TO DENTAL CARIES

A. In Areas where Fluoride Occurs Naturally

The low incidence of dental caries found among children living in communities whose natural water supplies contain fluoride has been clearly demonstrated by the epidemiological studies of Dean and his co-workers (Dean et al, 1941 and 1942). See Table II on page 27. The optimal concentration of fluoride (F) which affords maximum protection against dental caries with a minimum amount of dental fluorosis appears to be about 1 p.p.m. (Figure 1 - see page 32). Beyond this level there is little improvement in caries protection, and above 2 p.p.m. most of the children begin to show observable fluorosis (Dean, 1942).

It has been repeatedly demonstrated that children who have consumed fluoride free water all their lives experience almost twice as much dental decay as those children whose natural water supply contains traces of this element (Figure 2 - see page 33). This protection against dental caries due to the ingestion of the required trace of fluorides extends into adult life, (Russell and Elvove, 1951). See Table III on page 28.

Since the shedding of deciduous teeth and the development and eruption of the permanent teeth is a continuous process extending up to about the 20th year of life, and because some topical effects from the passage of fluoride-bearing water over the teeth are evident, the benefits of water fluoridation are not confined to the native born population (Klein, 1948). The maximum protection is of course obtained by individuals of continuous residence.

B. In Areas Where Fluoride is Added

As early as 1945, certain communities - Brantford, Ontario (Hutton et al 1951; Brown, H.K., 1952, 1953, 1956), Newburgh, New York (Ast, D.B. et al, 1951 and 1956) and Grand Rapids, Michigan (Arnold et al, 1956) - adjusted the fluoride content of their water supplies by using fluoride salts fed by an automatic mechanical apparatus. These devices simulate and improve upon the process by which natural water supplies pick up their fluoride salts from the subterranean deposits of natural fluoride-bearing chemicals.

The ten year reports summarizing the major findings of these studies have been published. All three reports conclude that the effect of controlled fluoridation has been to markedly reduce the dental caries attack in the primary and permanent teeth to the level observed in natural fluoride-bearing regions. The percentage reduction in decayed, missing and filled teeth has been approximately 60 per cent in residents who consumed fluoridated water during the development of their teeth. See Table IV on page 29 for a detailed analysis of the reduction in dental caries in these areas.

A recent survey completed by the U.S. Division of Dental Public Health (1957) indicates that a net total of 1,487 communities with over 31 million people were served by 680 water supply systems to which fluoride had been added. The survey reveals that approximately one out of every four persons using central water supplies was drinking fluoridated water with an adjusted fluoride content. In Canada 928,000 persons are benefiting from communal water fluoridation programmes or approximately one out of every nine persons who use central water supplies (Canadian Dental Association, 1957).

Publications in the U.S. Public Health Reports (1957) indicate

beneficial posteruptive effects of fluoridated water on caries of older children. In Grand Rapids it has been reported that for 16-year old children the DMF rate decreased 26 per cent between 1944 (the year before fluoridation was started) and 1954.

Hayes et al studied a group of children in Grand Rapids who had ingested fluoridated water since 1945 and in Muskegon, Michigan where fluoridation was started in 1951. All the children studied had two or more first permanent molars in 1944-45, and were continuous residents of their respective cities. The study groups, each composed of 116 children, were matched for caries susceptibility according to the 1944-45 examination. The mean age of the children from Grand Rapids was 6.52 and those from Muskegon 6.57 years. Between 1944-45 and 1956, the children of Grand Rapids experienced fewer and smaller cavities in proximal surfaces of first permanent molars than did the children of Muskegon. The mean caries score for proximal surfaces of first permanent molars for the two groups of children are summarized in Table V. The findings support the hypothesis that ingestion of fluoridated water will inhibit caries in teeth that have erupted prior to fluoridation. The finding that fluoride is readily incorporated into enamel posteruptively (Brudevold et al) supports the above hypothesis.

IV. MECHANISM BY WHICH FLUORIDES REDUCE DENTAL CARIES

There are at least two possible mechanisms by which fluoride may protect teeth against dental caries:

(1) Fluoride enters the structure of enamel apatite and forms fluorapatite (McCann, 1953).

Incorporation of fluoride into the tooth substance makes the tooth more resistant to acid etching . (Suess and Fosdick, 1951).

(2) Bacteria are known to be involved in dental caries (Orland et al 1954). Fluoride in suitable concentrations inhibits many bacterial enzymatic reactions (Bibby and Van Kesteren, 1950). Liberation of fluoride ion from the tooth substance may inhibit certain bacteria from participating in the dental caries process. No conclusive evidence for this mechanism is available.

V. METABOLISM OF FLUORINE

A. Fluorine Content of Body Fluids and Tissues

(1) Bones and Teeth

The dental tissues and the skeletal system are the major storehouse for fluorine in the body. Klement (1938) states that bones of animals (including man) average 0.05 per cent fluorine in inorganic bone material. There is a strong possibility that a 'normal' increase in the flourine content occurs in skeletal tissues and perhaps in dental tissues, with increasing age. The normal fluorine content of ribs is 0.03 to 0.14 per cent fluorine. Roholm (1937) showed that the fluorine content of the ribs of two cryolite workers (age 68 and 52) exposed to factory dust for 15 years and 8 years respectively equalled 0.65 - 0.72 per cent. Wolff and Kerr (1938) found that long bones of individuals with non-disabling fluorosis contained 0.18 - 0.29 per cent of fluoride. They concluded that the skeletal tolerance was of the order of 0.2 - 0.3 per cent of fluoride.

(2) Placenta and Mammary Secretion

Fluorides penetrate the placental barrier in small amounts only; the amount in mammary secretion is very low. According to Gardner (1952) fluorides are concentrated in the placenta. The fluoride value of 2.09 p.p.m. was found in placental tissue obtained from an area where the fluoride content of water is 1.2 p.p.m. This is compared to a value of 0.74 p.p.m. in the placental tissue obtained from areas where the fluoride concentration in water is 0.05 p.p.m.

(3) Saliva

Available evidence indicates that the excretion of fluorine through saliva is not of major importance. When radioactive fluorine is injected into the blood stream only trace amounts appear in the saliva (Wills, 1940). The flourine content of saliva is in the order of 0.1 p. p. m. and is not influenced by

the fluorine content of drinking water up to 1.8 p.p.m. (Cox, 1952).

(4) Urine

According to McClure (1947) there is a very efficient elimination of fluorine by way of the urine. When 3.0 - 4.0 mg. of fluorine were ingested daily more than 90 per cent was eliminated by the kidney in healthy adults. The average urinary fluoride excretion by groups of young men closely approximates the concentrations that were found in the water they drank over the range of 0.2 to 4.7 p.p.m. (See Table VI on page 31). Studies by Largent (1952) indicate that the amount of fluoride excreted by the kidneys appears to be related to the amount of fluoride previously stored.

The extraordinarily high urinary secretion of fluoride is attributable to a low resorption mechanism (for fluoride) in the kidney tubule. (Chen., 1955).

(5) Sweat

McClure (1946) found that in a group of five young men (19 - 24 years) who was given 3.0 mg. fluorine daily, undiluted sweat contained from 0.5 - 1.8 p.p.m. fluorine. Machle and Largent (1943) found an average of 0.514 - 0.0666 p.p.m. fluorine in perspiration. This evidence suggests that sweat and insensible perspiration may account for an appreciable loss of fluorine from the body.

(6) Fluorine in Blood

A 23-fold increase in fluoride content of drinking water (0.06 - 1.36 p.p.m.) results in a 3-fold increase of blood fluorine. The maximum observed level was 0.1 p.p.m. (Smith, Gardner and Hodge, 1950).

V. METABOLISM OF FLUORINE (cont'd)

B. Balance Studies

Heyroth's (1952) data indicates that adults are in metabolic balance with respect to fluoride when the daily ingestion of fluoride is 0.44 to 0.72 mg. per day. McClure (1946) states that in young adult men there is no significant retention of fluorine when the total daily fluorine ingested did not exceed 4.0 to 5.0 mg. daily.

Retention of fluoride in babies and young growing children is a subject that has not received much study. Balance studies by Ham (1952) were carried out in five young infants. The studies indicated that the fluorine in the infants' diet was retained to some extent. The per cent retention was influenced considerably by the fluorine content of the food consumed.

The stabilization of the fluorine concentration of the total ash of rats is a significant finding in relation to metabolism of fluorine. When rats are fed a ration containing a constant proportion of fluorine, the element accumulates during the first six months, after which the level of total fluorine in the rat carcass is not further increased even though the ration is still consumed for a year longer (Jackson, 1955).

VI. THE TOXICITY OF FLUORIDES IN POTABLE WATER SUPPLIES

Two aspects of this problem require consideration. One aspect is acute poisoning resulting from ingestion of large single doses of fluorides; the other is the effects of a long term ingestion of small amounts of fluoride as contained in potable waters. The former is a situation that may affect a single person or at most a very small group, whereas the latter is a public health problem.

A. Acute Toxicity

Examination of the phenomena of acute toxicity from fluorine is of value only as a possible aid in revealing what tissues or organs are most vulnerable to fluorine.

Fluorides in relatively large doses are highly toxic. Roholm (1937) estimated that the lethal dose of sodium fluoride for man was four grams. Acute symptoms may be caused by 250 mg. of sodium fluoride (Cox and Ast, 1951).

The high dosages necessary for acture fluoride poisoning could not be obtained as a result of accidental or deliberate over-fluoridation of water supplies. In order to obtain acute toxic effects it would be necessary to dump approximately eight tons of sodium fluoride into the Brantford water supply in one day. The amount actually used in the Brantford supply is about 140 pounds in one day.*

B. Chronic Toxicity

(1) Bones and Teeth

Moller and Gudjonsson (1932) in an examination of 78 cryolite (sodium aluminum fluoride) workers found that 30 complained of stiffness and

* (Based on a 5,000,000 Gallon consumption)

pain and showed x-ray evidence of osteosclerosis. It was estimated that 14 to 25.4 mg. of fluorine in dust was inhaled daily. The average deposition of fluoride was about 12 mg. per day absorbed over a period of more than 20 years. Autopsy examination of two persons who died of intercurrent disease showed osteosclerotic changes in the bones. No histopathological changes were observed in other organs.

Endemic skeletal fluorosis has been reported from China in malnourished persons who used water containing 5.9, 6.3 or 13.1 p.p.m. of fluoride (Lyth, 1946).

McClure (1946) in an examination of 1400 high school boys and 1700 draftees grouped according to fluoride exposure levels (0 to 1. p.p.m) in the water supply, found no significant differences in the numbers of bone fractures.

Hodges (1941) in a study of 31 persons who lived for 18 to 68 years at Bureau, Illinois, where the water contained 2.5 p.p.m. of fluorine found no evidence of skeletal fluorosis.

Children drinking waters containing 1 p.p.m. of fluoride have less than 10 per cent of their number develop a very mild degree of dental fluorosis. This is the earliest clinical manifestation of exposure to fluorides. It will not cause staining of the teeth and is not detrimental to their appearance.

(2) Other Tissues and Organs

McClure (1946) found that the data on stature and weight of young children and adolescents in fluoride and non-fluoride areas (up to 1.8 p.p.m.) revealed no differences. Pediatric studies in the Newburgh-Kingston area, including complete physical examination, blood and urine analysis, x-rays of hands, forearms and tibia and special eye and ear examinations revealed no

significant differences in any of the factors studied in children in the fluoride and non-fluoride areas (Schlesinger et al, 1953) This study covers a period of six years since introduction of fluoride into the Newburgh water supply.

The Wisconsin State Board of Health (1942) investigated the relative number of deaths from cancer, heart disease, nephritis and other illnesses in cities with varying concentrations of fluoride in the water. No significant differences were observed in areas where the fluoride ranged from 0.02 to 2.5 p.p.m.

Leone et al (1955, -article reprinted in Appendix II) reported on a ten year study of a population group which had ingested water containing excessive amounts of naturally occurring fluoride (8 ppm). This group was compared to persons who lived in a neighboring city with a water supply that contained 0.4 ppm of fluoride. The 237 individuals studied were evenly divided between the two groups. The average length of residence was 37.5 years for the two groups. The subjects' ages ranged from 15 to 68 years at the beginning of the study. Analysis of the data produced the following conclusions:

(a) The two groups showed no significant differences in the ten year period with respect to changes in blood pressure, arthritic conditions, eyes, thyroid disorders, hearing, tumors, cysts, bones and bone fractures, and the urinary system.

(b) The incidence of cardiovascular disease was higher in the area containing 0.4 ppm of fluoride, an observation unrelated to fluoride ingestion.

(c) There were no significant differences between the age-adjusted death rates in the two towns.

(d) The only difference in laboratory findings was in the white blood cell count, which tended to be higher in the fluoride area in 1953. White blood cell counts are normally subject to considerable variation and, when viewed in the light of clinical experience, this finding does not suggest an association with fluoride intake.

The data indicate that except for dental fluorosis the medical characteristics of the two groups do not differ significantly.

This study was extended to include a roentgenologic study (Leone, et al, 1955) of a human population exposed to high-fluoride domestic water. The data based on a study of 237 cases "demonstrate that except for dental mottling, ingestion of water containing fluorides up to 8 ppm produces no deleterious bone changes: no unusual incidence of bone fracture, arthritis, hypertrophic bone changes or exostoses, or interference with fracture healing; no cases of "poker" spine and no evidence of associated functional or systemic effects". It was noted "that the ingestion of excessive fluoride in water ... may, on occasion, have a beneficial effect in adult bone, as in counteracting the osteoporotic changes of the aged".

Because of the chemical relationship between fluorine and the halogen group of elements, its possible effect on thyroid function has been studied. A study by Evans and Phillips (1938) revealed no correlation between the fluorine content of the thyroid gland and the basal metabolic rate of the patient. No relationship was observed between the iodine and fluorine content of these thyroids. The data gave no indication that fluorine played a part in human hyperthyroidism.

(3) Fluorides and Periodontal Disease

Studies directed to an examination of the relationship of ingestion of fluorides in water to periodontal and gingival conditions permit the following conclusions:

(1) Persons in an age group of 40-44 years residing since birth in areas where the fluoride content of water was negligible have lost four times as many teeth as persons of the same age group living in areas where the fluoride content in the water supplies is 2.5 ppm. (Russell and Elvove, 1951).

(2) There is no significant difference in the prevalence of gingivitis between persons (mean age 57.1) residing in an area which contains 8.0 ppm of fluorides and those (mean age 55.3) living in an area with a fluoride-free water supply (Zimmermann, 1955). The presence of 1 ppm fluoride in drinking water had no effect on the gingivitis of children (age 6 to 14) (Brown et al., 1952).

(3) There is no significant difference in the amount of calculus formation and alveolar bone resorption among residents (mean age 57.1) living in an area containing 8 ppm of fluoride and the residents (mean age 55.3) of an area with fluoride-free water (Zimmermann, 1955). The average length of residence of the two groups in these areas was 37 and 38 years respectively.

(4) A radiographic study of rats on a fluorine-free diet (McClendon and Gershon - Cohen, 1954) revealed extensive periodontal disease in the molar regions and freedom from these defects in rats receiving 10 ppm fluorine in drinking water. The evidence suggests that fluorine may be an essential trace element for optimal nutrition in rats.

(5) Russell (1957) reports that the use of fluoride-bearing water does not adversely affect the prevalence or severity of periodontal disease in children or adults. The study was made on a total of 20,000 persons comprising three groups. One of the comparisons was between 144 adults aged 20-44 in Colorado Springs (2.5 ppm F) and 379 adults of the same age group in Boulder (fluoride-free). For older adults a comparison was made between residents of Bartlett (8.0 ppm F) and those of Cameron (0.4 ppm F). Comparisons for children were made between residents of Newburgh (1 ppm F) and Kingston (fluoride-free). In addition, 18,000 natives and migrant children in communities using water containing about 1.0 ppm F were compared. In each of the above studies the fluoride group exhibited the more favourable periodontal condition. Extractions as a result of periodontal disease were somewhat less frequent among adults in the fluoride communities.

VII. TECHNICAL PROCEDURES OF WATER FLUORIDATION

The local water works staff in consultation with their provincial government authorities are qualified to determine the fluoride compound and chemical feeding apparatus most suitable for a particular municipality's needs. The technical problems have been well discussed by the following authors:

H.F. Munroe (1953); Maier, (1952); Robertson, (1952); and Williams, (1951).

VII. LIST OF NATIONAL HEALTH ORGANIZATIONS WHICH HAVE ENDORSED FLUORIDATION

Canada

Canadian Dental Association

Canadian Medical Association

Canadian Public Health Association

Canadian Society of Dentistry for Children

The Dental Public Health Committee of the Ontario Dental Association

The Executive Council of the Toronto Academy of Dentistry

The Health League of Canada

The Ontario Public Health Association

Toronto Academy of Medicine

United States

American Academy of Pediatrics

American Cancer Society

American Dental Association

American Hospital Association

American Medical Association

American Nurses' Association

American Public Health Association

American Society of Dentistry for Children

The Commission on Chronic Illness

National Research Council (U.S.A.)

State and Territorial Dental Health Directors

State and Territorial Health Officers Association

United States Public Health Service

United States Department of Health, Education and Welfare.

IX. STATEMENT OF THE CANADIAN DENTAL ASSOCATION ON FLUORIDATION

Whereas tooth decay, by affecting the vast majority of people in Canada, has come to be recognized as one of the major public health problems of our time, and

Whereas studies covering a period of over thirty years under the widest variety of controlled conditions have marked fluoridation as one of the most widely studied of public health procedures, and

Whereas such studies reveal that fluoride in the recommended amount of 1 part of fluoride to 1 million parts of water is safe from any ill-effect and is effective in reducing tooth decay by approximately two-thirds, and

Whereas fluoridation benefits children and the benefits extend into adult life, therefore be it

> Resolved, that the Canadian Dental Association reiterates its recommendation to the people of Canada that communities having a public water supply adopt a procedure for adjusting the fluoride content of their water supply, and for this purpose seek competent dental, medical and engineering advice.

X. MUNICIPALITIES WHICH HAVE FLUORIDATED WATER SUPPLY

As of January 1957

Municipality	Date When Started	Population
Newfoundland		
none		
Prince Edward Island		
none		
Nova Scotia		
Halifax	June 11/56	90,871
Dartmouth	July 3/56	20,004
Kentville	Feb. 16/56	4,840
New Brunswick		
none		
Quebec		
Point Claire	Feb. 3/55	15,067
Sillery	Oct. 19/55	13,800
Ontario		
Brantford	June 20/45	51,557
Brockville	Feb. 18/56	15,000
Deep River	Dec. 9/52	3,000
Fort Erie	Jan. 18/52	8,567
Oshawa	Feb. 26/53	50,136
Sudbury	Aug. 29/52	60,000
Thorold	Feb. 12/52	8,001
Tisdale Township	Oct. 3/55	8,000
Manitoba		
Brandon	March 8/55	24,579
Winnipeg	Dec. 28/56	409,687
Saskatchewan		
Assiniboia	May 1953	2,500
Moose Jaw	December 1952	29,282
Saskatoon	July 1955	70,843
Swift Current	October 1954	10,468
Weyburn	March 1955	7,616
Wynyard	August 1956	1,492
Alberta		
none		
British Columbia		
Kelowna	Sept. 15/56	8,924
Prince George	Sept. 13/56	12,500
Smithers	June 21/55	1,936
TOTAL		928,665

XI. SUMMARY

1. Most natural water supplies and many different foods contain fluorine. The most significant source of fluorine from a standpoint of human consumption is water. Concentration of fluorine in water may vary from traces to excessive amounts. Populations in many parts of the world have for centuries been drinking water in which fluoride occurs naturally.

2. There is approximately a 60 per cent reduction in dental caries where a desirable amount of fluoride ion, whether naturally occurring or the result of supplement, exists in the drinking supply. The desirable concentration of fluorine in water, based on its ability to reduce the incidence of dental caries without any undesirable effects, is in the order of one part of fluoride ion per one million parts of water. Higher concentrations of fluorine produce no added reduction in dental caries but result in dental fluorosis.

3. There is no evidence of detrimental effects on the health of individuals drinking water containing fluorine at the level of intake of 1 p.p.m. Studies of vital statistics of common major diseases, and of maternal and newborn death rates, all confirm the safety of a fluoridation program.

4. Most of the fluoride consumed at the level of 1 p.p.m. is excreted by the kidneys and sweat. A minimal amount, far below the fluorosis threshold, is stored in bones and teeth.

5. Most health organizations of recognized scientific standing have endorsed the efficacy and safety of fluoridation. A recent survey indicates that a total of over 31,000,000 persons in over 1487 communities, or approximately one out of four persons, in the United States, is served by fluoridation programs.

6. Scientific studies offer an impressive body of evidence that 'bringing the fluoride concentration in communal water supplies to that known to be optimal for dental health is a prophylactic public health measure which has an ample margin of safety.'

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TABLE I

FLUORINE CONTENT OF FOODS

Food	Fluorine, parts per million	Food	Fluorine, parts per million
Fluorine reported in food as consumed			
Milk	0.07-0.22	Pork Chop	1.00
Egg white	0.00-0.60	Frankfurters	1.70
Egg yolk	0.40-2.00	Round steak	1.30
Butter	1.50	Oysters	1.50
Cheese	1.60	Herring (smoked)	3.50
Beef	<0.20	Canned shrimp	4.40
Liver	1.50-1.60	Canned sardines	7.30-12.50
Veal	0.20	Canned salmon	8.50- 9.00
Mutton	<0.20	Fresh fish	1.60- 7.00
Chicken	1.40	Canned mackerel	26.89
Pork	<0.20		
Fluorine reported in dry substance of food			
Rice	<1.00	Honey	1.00
Corn	<1.00	Cocoa	0.50- 2.00
Corn (canned)	<0.20	Milk chocolate	0.50- 2.00
Oats	1.30	Chocolate (plain)	0.50
Crushed oats	<0.20	Tea (various brands*)	30.00-60.00
Dried beans	0.20	Cabbage	0.31- 0.50
Whole buckwheat	1.70	Lettuce	0.60- 0.80
Wheat bran	<1.00	Spinach	1.00
Whole wheat flour	1.30	Tomatoes	0.60- 0.90
Biscuit flour	0.00	Turnips	<0.20
Flour	1.10-1.20	Carrots	<0.20
White flour	1.00	Potato (white)	<0.20
Ginger biscuit	2.00	Potato (sweet)	<0.20
Rye bread	5.30	Apples	0.80
Gelatin	0.00	Pineapple (canned)	0.00
Dextrose	0.50	Orange	0.22

* Analysis of tea leaf. A cup of tea contains about 0.12 mg. of fluorine.

Source: McClure, F.J., National Inst. of Health Bulletin, 172, 1939.

TABLE II

Summary of Dental Caries Findings in 7,257 Selected White School Children
Age 12 to 14 years, in 21 cities of 4 States
in Relation to the Fluoride (F) Content of the Public Water Supply

City and State	No. of Children Examined	Percent of Children Caries Free	No. of D.M.F. Teeth per Child with Caries Experience	F. Conc. (p.p.m) Public Water Supply
Galesburg, Ill.	273	27.8	2.36	1.9
Colorado Springs, Colo.	404	28.5	2.46	2.6
Elmhurst, Ill.	170	25.3	2.52	1.8
Maywood, Ill.	171	29.8	2.58	1.2
Aurora, Ill.	633	23.5	2.81	1.2
East Moline, Ill.	152	20.4	3.03	1.2
Joliet, Ill.	447	18.3	3.23	1.3
Kewanee, Ill.	123	17.9	3.43	0.9
Pueble, Colo.	614	10.6	4.12	0.6
Elgin, Ill.	403	11.4	4.44	0.5
Marion, Ohio	263	5.7	5.56	0.4
Lima, Ohio	454	2.2	6.52	0.3
Evanston, Ill.	256	3.9	6.73	0.0
Middletown, Ohio	370	1.9	7.03	0.2
Quincy, Ill.	330	2.4	7.06	0.1
Oak Park, Ill.	329	4.3	7.22	0.0
Zanesville, Ohio	459	2.6	7.33	0.2
Portsmouth, Ohio	469	1.3	7.72	0.1
Waukegan, Ill.	423	3.1	8.10	0.0
Elkhart, Ind.	278	1.4	8.23	0.1
Michigan City,	236	0.0	10.37	0.1

Source: Dean, H.T., et al, 1941

TABLE III

Comparison of Average No. of Decayed, Missing and Filled Permanent Teeth in Adult Natives of Boulder, and Colorado Springs, Colorado, excluding third Molars.

Age Group Years	Boulder (F concentration . 1 ppm)		Colorado Springs (F concentration 2.5 ppm)		Per Cent reduction in Colorado Springs
	Number of Persons	Mean no. of D.M.F. Teeth *	Number of Persons	Mean no . of D.M.F. Teeth *	
20-24	51	13.8	72	5.2	62.3
25-29	41	16.0	101	6.2	61.2
30-34	29	16.3	82	6.7	58.3
35-39	22	20.4	75	7.6	62.7
40-44	12	19.1	55	8.7	54.5

* Decayed, Missing or Filled Teeth omitting loss due to periodontal Disease and accidents

Source: A.L. Russell and E. Elvove (1951)

TABLE IV

RESULTS OF MAJOR FLUORIDATION STUDIES

City	Report Period	Age in Years	Per Cent of Reduction in Decayed, Missing and Filled Teeth. Perm.	Primary
Brantford, Ontario Canada	1945-1956	6 - 8	51	40
		9 - 11	44	16
		12 - 14	37	
Evanston, Illinois	1947-1955	6	85.9	35.9
		7	73.3	26.3
		8	54.3	18.4
	After 47-58 months	12 - 14	18.5	
Grand Rapids, Michigan	1945-1955	4		50
		5		53
		6	75	54
		7	63	47
		8	57	
		9	49	
		13	48	
		16	25	
			Per Cent K - N	Difference
Newburgh and Kingston (Sodium fluoride added to Newburgh water supply May 1945)	For Primary Teeth 1945-1955	6		60
		7		46
		8		28
		9		19
	For Permanent Teeth 1944-1955	6 - 9	58	
		10 - 12	53	
		13 - 14	48	
		16	41	

TABLE V

Mean Caries-Scores for Approximal Surfaces Becoming Decayed or filled Between 1944-1945 and 1956; First Permanent Molars Erupted in 1944-1945, Grand Rapids and Muskegon

	X-Rays Only			Clinical: Clinical + X-Ray	
	Total Group	Unmatched	Matched Group	Matched Study Group	
Muskegon	1.99	1.97	1.99	1.22	2.02
Grand Rapids	1.67	1.57	1.73	0.83	1.74
Difference	0.32	0.40	0.26	0.39	0.28
Standard Error of Difference	. . .	. . .	0.12	0.11	0.12

Hayes et al, Amer. J. Pub. Health 47;192, 1957.

TABLE VI

FLUORINE CONTENT OF URINE STUDIED IN RELATION TO FLUORINE IN FLUORIDE DRINKING WATER

Location	Fluorine in water	Fluorine in urine	Number of specimens represented	Comment
	ppm	ppm		
Amarillo, Texas	4.7	4.6	26	High school boys age 16-18
Amarillo, Texas	4.7	4.0	42	Selectees, Lubbock induction center
Airfield, Lubbock, Texas	5.1	4.0	50	Service men stationed at airfield
Lubbock, Texas	3.8	3.8	52	High school boys age 16-18.
Lubbock, Texas	3.8	4.2	21	Texas Tech. College men age 17-21
Lubbock, Texas	3.8	3.7	108	Selectees, Lubbock induction center
Glider field, Lubbock, Texas	2.0	2.0	16	Service men stationed at Glider field
Galesburg, Ill.	1.9	1.8	173	High school boys age 15-17
Monmouth, Ill.	1.7	1.4	156	High school boys age 15-17
Joliet, Ill.	1.3	1.0	21	Selectees, Chicago induction center.
Aurora, Ill.	1.0	0.9	170	High school boys age 15-17
Elgin, Ill.	0.7	0.7	170	High school boys age 15 - 17
Rural central Ind.	0.5*	0.7	109	Selectees, Indianapolis induction center
Oklahoma City, Okla	0.5	0.6	26	High school boys age 16-18
Indianapolis, Ind.	0.2	0.4	121	Selectees, Indianapolis induction center
Chicago, Ill.	0.1	0.3	60	Selectees, Chicago induction center
Quincy, Ill.	0.1	0.3	85	High school boys age 15-17
Washington, D.C.	0.0	0.4	202	Selectees, Ft. Myer induction center
Washington, D.C.	0.0	0.3	65	High school boys age 15-17
Little Rock, Ark.	0.0	0.3	26	High school boys age 15-18
Waukegan, Ill.	0.0	0.4	144	High school boys age 15-17
New Hampshire	0.0	0.3	174	Selectees, Manchester induction center

*Estimated average for fluorine in waters at this area

Source: McClure, 1946, National Institute of Health, Division of Physiology Dental Research Section, Bethesda, Maryland.

FIGURE I

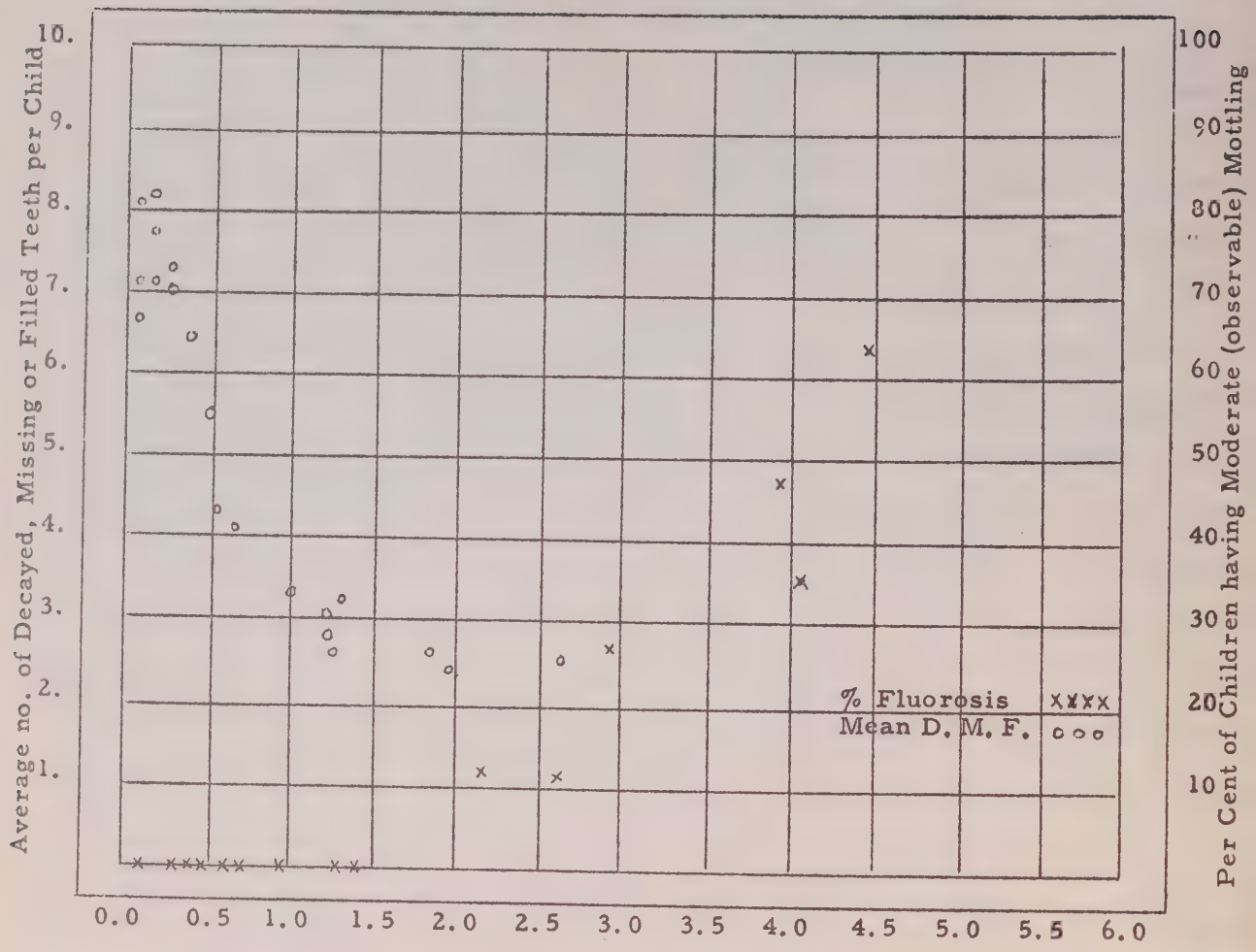

Figure 2. Relationship of Fluoride (F) control of Public Water Supply in p.p.m. the average number of decayed, missing and filled teeth per child, age 12 to 14 years and the prevalence of moderate, (observable) brown mottling among children age 9 to 12 years in cities of U.S.A.

Source: H.T. Dean, 1941, and Dean et al, 1941, 1942.

FIGURE 2

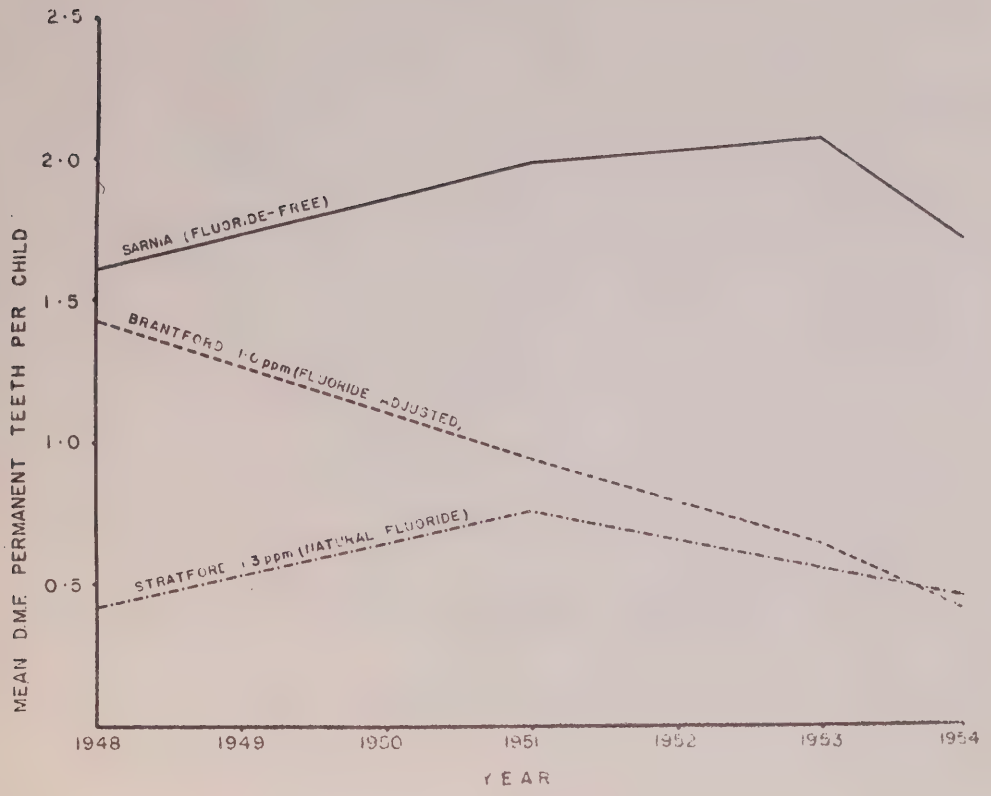

Figure 2 - Mean DMF permanent teeth per child in 6 - 8 year age group in non fluoride (Sarnia), adjusted fluoride (Brantford), and natural fluoride (Stratford) areas, over a nine year period.

The first permanent molars of the Brantford children born subsequent to the initiation of fluoridation in 1954, appear to show a resistance to caries comparable to that of the teeth of the children of the same age group in Stratford where the water has contained 1.3 p.p.m. of fluoride since 1917.

Data obtained from Brantford fluoridation caries study - 1954 report, Table 4, H.K. Brown, H.R. McLaren and B. Stewart: J. Can. Dent. Assoc. 20 (11):585. 1954

APPENDIX 1

LIST OF SOME AREAS IN CANADA

CONTAINING NATURAL FLUORIDE

IN MUNICIPAL WATERS

AMOUNTS OF NATURAL FLUORIDE IN MUNICIPAL WATERS

Place	Year	Source	Fluoride Content ppm*
Province of British Columbia			
Bralorne, B.C.	1952		0.1
Boston Bar, B.C.	1946	Stoyoma Creek	0.01
Cloverdale, B.C.	1952		1.2
Creston, B.C.	1947	Arrow Creek	0.1
Enderby, B.C.	1948		0.25
Fort Steel, B.C.	1949		0.1
Fort St. John, B.C.	1949	Charlie Lake	0.02
Kelowna, B.C.	1952	North Okanagan Lake	0.2
Kimberley, B.C. (airport)	1949	Deep Well	0.07
McBride, B.C.	1948	Dominion Creek	0.10
North Vancouver, B.C.	1949	Lynn Creek	0.05
North Kamloops, B.C.	1948	South Thompson River	0.07
Oliver, B.C.	1950	Shallow Well	0.5
Summerland, B.C.	1950	Headwaters Lake	0.2
Sidney, B.C.	1948	5 Wells and a spring	0.25
Trail, B.C.	1949	Columbia River	0.1
Vernon, B.C.	1948	Kalamalka Lake and mountain springs	0.1
Williams Lake, B.C.	1950		0.1
Yale, B.C.	1949		0.03
Province of Alberta			
Beaver River, Alta.			0.1
Bonnyville, Alta.		Shallow Well	0.35
Cardston, Alta.		From River	0.3
Lacombe, Alta.		Deep Well	1.0
Mirror, Alta.		Well	0.5
Saunders Lake, Alta.			0.4
St. Paul, Alta.			0.07
Province of Saskatchewan			
Prince Albert, Sask.		North Saskatchewan River	0.12
Shaunavon, Sask.		Well	0.1
Swift Current, Sask.		Swift Current Creek	0.25
Weyburn, Sask.		Souris River	0.18
Yorkton, Sask.		3 Wells	0.2
Province of Manitoba			
Winnipeg, Man.		Shoal Lake, Lake of the Woods	0.25

*Parts per million.

Place	Year	Source	Fluoride Content ppm.
Province of Ontario			
Alymer, Ont.		Well No. 2	1.0
Caledonia, Ont.		Wells (water softened)	0.60
Clinton, Ont.		Well	0.8
Coburg, Ont.		Springs	.05
Dresden, Ont.		Well	2.0
Dunnville, Ont.		Grand River	0.2
Essex, Ont.		Boone Well	2.5
Etobicoke Twp., Ont.		Deep Wells	.05
Fergus, Ont.		Well	0.6
Galt, Ont.		Civic Well	.38
Georgetown, Ont.		Deep Well	0.2
Gravenhurst, Ont.		Wells	.21
Guelph, Ont.		Park Street Well	0.3
Hamilton, Ont.		Lake Ontario	0.1
Hagersville, Ont.		Deep Well	1.2
Ingersoll, Ont.		Springs	0.05
Kitchener, Ont.		Wells	.05
Leamington, Ont.		Wells	0.5
Lindsay, Ont.		Scugog River	.07
London, Ont.		Norton St. Well	0.7
London, Ont.		(Springs) Springback	0.1
London, Ont.		Foster Wells	0.3
Lucknow, Ont.		Wells	2.0
Meaford, Ont.		Georgian Bay	0.1
Niagara-on-the-Lake, Ont.		Niagara River	0.1
North York Twp., Ont.		Well Plant No. 2.	0.05
Oakville, Ont.		Lake Ontario	.08
Orillia, Ont.		Well	.05
Oshawa, Ont.		Lake Ontario	.10
Paris, Ont.		Springs	.05
Peterborough, Ont.		Otonabee River	.07
Petrolia, Ont.		Lake Huron	0.05
Port Colborne, Ont.		Lake Erie	0.15
Port Dover, Ont.		Springs	0.1
Port Credit, Ont.		Lake Ontario	0.1
Port Elgin, Ont.		Wells and Springs	0.2
Preston, Ont.		Well No. 2	0.1
Ridgetown, Ont.		8 Wells	1.2
Scarborough Twp., Ont.		Lake Ontario	0.09
Seaforth, Ont.		Wells	0.8
Shelburne, Ont.		Well	1.5
Simcoe, Ont.		Wells and Springs	0.1
Sioux Lookout, Ont.		Pelican Lake	0.05
South River, Ont.		Springs	0.1
Stamford Twsp., Ont.		Wells	0.1
St. Catherines, Ont.		Welland Canal	0.1
St. Thomas, Ont.		Kettle Creek	.25
Stirling, Ont.		(Gravel and Sand) Well	0.25
Stirling, Ont.		Rock Well	0.15
St. Mary's Ont.		Wells	1.0

Province of Ontario (Cont'd)

Place	Year	Source	Fluoride Content ppm.
Stratford, Ont.		Wells	1.6
Tara, Ont.		Well	.80
Tavistock, Ont.		Spring,	0.05
Tecumseh, Ont.		Detroit River	0.1
Teeswater, Ont.		Artesian Well	0.5
Thornbury, Ont.		Beaver River	0.10
Thorold, Ont.		Welland Canal	.15
Thorold Twsp., Ont.		Welland Canal	0.05
Tilbury, Ont.		Lake St. Clair	0.05
Tillsonburgh, Ont.		Two gravel wells	0.15
Trenton, Ont.		Springs and Wells	.05
Tweed, Ont.		Foster Dairy Well	.05
Uxbridge, Ont.		Wells	.04
Walkerton, Ont.		Wells and Springs	1.5
Waterloo, Ont.		Seagram Well	0.40
West, Ont.		Lake Erie	0.4
Woodstock, Ont.		Gravel Wells	.15
Later Analysis			
Ingersoll, Ont	1953	(a) Well	1.8
		(b) Well	1.8
St. Mary's, Ont.	1953	Well	1.2
Woodstock, Ont.	1953	(a) Well	0.3
		(b) Well	0.3
		(c) Well	0.3

Source: Department of National Health and Welfare, Ottawa, Canada.

26 August 1953.

APPENDIX II

REPRINTS

THE TOXICITY OF FLUORIDES IN RELATION TO THEIR USE IN DENTISTRY

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It has been our purpose to review the toxicology of fluorides only in the aspects related to dental health. The list of dental uses of fluorides is growing and has already included the following surprisingly large number of items: (1) Fluoridization of water and related pre-eruptive procedures for the prevention of dental caries. (2) Topical application of fluorides for control of dental caries. (3) Fluoride pastes to desensitize dentin. (4) Toothpastes and powders. (5) Mouth wash. (6) Fluoride plus vitamin tablets. (7) Chewing gum.

With the increased use of fluorides, it is proper to insist that due attention be paid to the possible hazards and to insist that there be a large factor of safety. Fluorine and its compounds have long been known as poisons. In the following discussion, the toxic effects of fluoride are grouped under four main headings: Acute Poisoning, Chronic High-Grade Poisoning, Chronic Low-Grade Poisoning, and Local Action. In each case, after the toxic effects have been described, an evaluation has been made of the possibility of such effects appearing in conjunction with the use of fluorides in dentistry.

It is our intent to indicate the safety of the therapeutic uses of fluorides, and it is not our intent to warn against the uses of fluorides in dentistry. This discussion, however, should alert the users to the dangers of carelessness and misuse, dangers to both the subjects and the operators.

Objections to the uses of fluorides in dentistry have come from various sources. These have been mainly from the specialists in various fields who are uninformed about the proved possibilities of fluorides. Those who have competing procedures have advanced their wares by attacks on fluorides. Some who have seen only the bad effects of fluorides refuse to accept the good. There have been dire warnings of bad effects, characteristically naming nothing specific. It has been the vogue to proceed cautiously in the fluoridization of water and such caution implies more the fear of the unknown than doubt of the benefits.

The word "fluorine" as used in this paper refers to fluoride ions or the fluorine portion of a compound containing the element.

Extensive reviews of the toxicology of fluorine are available and many of the papers on mottled enamel and on dental caries present evaluations of the literature on fluorine toxicity. Symposia have dealt with the whole problem of fluorine in its relations to dental health with consideration of its toxicity, and McClure has summarized knowledge of fluoride effects published during the period 1934 through September 1948.

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The opinions expressed are those of the authors and do not necessarily reflect the opinions of the Council on Dental Therapeutics.

Acute Toxicity

Effects of Oral Doses on Man. --- Fluorides rank among the substances whose ingestion in small amounts can cause death within a few hours. Rabuteau administered sodium, potassium, ammonium and other fluorides to cats, dogs, rabbits and frogs and noted salivation and vomiting. For extension of the findings to man he took by mouth 0.25 gm. of sodium fluoride in 25 ml. of water. (This is a 1 per cent solution of sodium fluoride or approximately 4,500 ppm. as fluoride ion. It is approximately 1 fluidounce of half the 2 per cent strength recommended for topical application of fluorides.) He noted a slight nausea with epigastric sensations which lasted about five hours. Salivation was intense for about a half hour and noticeable up to one and one-half hours. He noted an itching sensation in trunk, hands and feet that lasted about a week. It is important to note that Rabuteau swallowed approximately 1 fluidounce of a 1 per cent sodium fluoride solution; that is, one of half the strength recommended for topical application of sodium fluoride.

Baldwin swallowed sodium fluoride experimentally, in increasing doses. He reported:

0.03 gm. swallowed with some bread produced no effect. Neither did 0.09 gm. taken one hour later, except a little salivation. 0.25 gm., however, taken two days afterward on an empty stomach, produced nausea in two minutes. This gradually increased in severity for twenty minutes when the period of greatest intensity was reached. There was a largely increased flow of saliva and some retching but no vomiting occurred at that time though the desire was very great. The nausea gradually subsided so that luncheon could be eaten (without relish), but no vomiting took place immediately on its completion which was two hours after taking the poison. Slight nausea continued throughout the following day but disappeared on the second day.

That Rabuteau and Baldwin were fortunate is indicated by the findings of Gettler and Ellerbrook. They analyzed the vital organs and tissues from five fatal cases of fluoride poisoning. Since all the materials were not submitted for analysis, they supplemented their data with analyses of tissues from dogs experimentally poisoned. They found the fluorine contents of the organs of the two species after acute fluoride poisoning to be within the same range and no difference whether death was caused by sodium fluoride or fluosilicate. The fluorine content of the urine was highly variable.

Following a brief review of estimates by others of the minimum lethal dose of fluorine they wrote:

The reason why such wide variations as to the lethal dose exists may be (a) the amount of fluorine actually taken by the subject is only a guess; (b) some of the ingested fluorine is lost in the vomitus; (c) the fluorine remaining in the gastro-intestinal tract (unabsorbed) has no bearing on the cause of death; that part of the poison which has been absorbed into the circulation and tissues is solely responsible for the death of the individual; (d) fluorine is very rapidly excreted in the urine.

Gettler and Ellerbrook then calculated from the analyses of human and dog tissues that death could be caused in a 140 pound man by absorption of as little as 105 mg. of fluorine. The dosage taken by mouth by both Rabuteau and Baldwin was approximately 110 mg; the amount absorbed is unknown.

Approximate Lethal Dose for Man --- It is unnecessary to stress the difficulty of estimating accurately the dose of fluoride to kill the average man. In animals, for example in the rat, the LD50 (dosage from which 50 per cent of the animals die) is of the order of 50 mg. per kilogram of body weight. Since fluoride is one of the general protoplasmic poisons, it may well be that an average fatal dose for man is of the same order of magnitude. It would be impossible to cite all of the estimated doses in fatal poisoning cases that have been recorded in the literature. In the brevity required by this review, instead, a few typical examples are cited in Table 1.

Table 1. --- Examples of the relation of various dosages of fluorides to the lethal dosage in man -

Probable dose	Effect	Compound
100 mg. or more	Death predicted	Sodium fluoride (fluosilicate)
0.2 - 0.6 Gm.	71 cases with recovery	Sodium Fluoride
0.7 --1.0 Gm.	Fatal	Sodium fluosilicate
1 Gm. or more	60 fatal cases 52 survived	Fluoride and Fluosilicate
5 Gm.	Fatal	Fluoride or Fluosilicate
5--9 Gm.	Recovery	Sodium fluoride
5--10 Gm.	47 fatal of 263 cases	Sodium fluoride
95 per cent paste in water, 50-80 Gm.	Recovery	Sodium fluoride

It is difficult to judge the minimum lethal dose from the above, mainly because the estimation of the doses is quite uncertain and fluoride has been ejected in unknown amount through vomiting. Roholm's opinion that 4 Gm. is the minimum amount of sodium fluoride known to have caused death of an adult has been widely accepted. Black, Kleiner and Bolker claimed that oral doses of 20 to 50 mg. of sodium fluoride given four times a day to children 3 1/2 to 6 years of age, or 80 mg. doses given four times a day to adults, were not toxic. The sodium fluoride was given with a suspension of aluminum hydroxide. Sharpless has shown that an aluminum salt fed in excess of sodium fluoride prevents mottling of the enamel of rat incisors. Black, Kleiner and Bolker stated "If taken alone, sodium fluoride causes gastritis and regurgitation.."

Mechanism of Acute Fluoride Poisoning. --- While the mechanism of acute fluoride poisoning is still obscure, studies from a variety of sources have indicated how some of the effects arise. The nausea, vomiting and the diarrhea in some cases may be attributed to the ingestion of the hypertonic salt solution which is irritating to the mucosa of the stomach. The local action of fluorides on the mucosal tissues certainly contributes to these effects.

When absorbed, fluoride forms strong complexes with calcium; for example, Rabinowitch described a case of suicide by ingestion of sodium fluoride. The subject did not vomit. He showed spasms of the hands and feet and died of respiratory failure three hours and five minutes after ingestion of the poison. A blood sample taken a few minutes before death showed 2.6 mg. of calcium per 100 ml. of serum, believed by Rabinowitch to be the lowest ever observed in man. Normal is 9 to 11.5 mg. The low blood calcium may be the basis for the twitchings observed in severely poisoned individuals.

Probably the most important actions of fluorides are those on enzymes. Some of the basic and necessary metabolic processes in the cell are stopped by concentrations of fluoride such as are found in acute poisoning. These changes are comparable to those seen in high-grade anoxia and are the basis for describing fluorides as general protoplasmic poisons.

Treatment of Acute Fluoride Poisoning. --- Roholm says of fluoride poisoning:

On the whole, the prognosis must be characterized as bad; the mortality is high. Whether or not there is vomiting is a matter of vital importance to the prognosis. It is presumable that the quantity and nature of the stomach contents also have some bearing. It is possible that an existing anacidity reduces the possibility of absorption and thereby improves the prognosis.

On the whole, no definitely effective treatment has been used. The rational therapy is intravenous injection of a soluble calcium salt, to which must be added gastric lavage and peroral administration of a solution of calcium chloride, perhaps milk. Treatment must be commenced quickly to have any chance of being effective.

For treatment of acute fluoride poisoning by mouth, Rabinowitch recommended thorough washing of the stomach with lime water or a weak solution of calcium chloride if lime water is not immediately available. If neither is available, water should be used repeatedly in small amounts. He recommended intravenous injection of a 10 per cent calcium gluconate solution without delay on appearance of any signs suggestive of tetany, or very cautious injection of a more dilute solution of calcium chloride if the gluconate is not immediately available.

Peters reported the case of a 16 year old girl who swallowed with suidical intent:

... about 4 ounces of a thicker-than-cream suspension of 95 per cent sodium fluoride in water (estimated to have been 50-80 gm.), the largest dosage from which a human has been known to receover. Undoubtedly early vomiting ejected much of this.

Peters stressed the use of lime water by gastric lavage and calcium gluconate for intravenous injection for relief of acute poisoning by ingested fluoride. He followed the suggestions of Rabinowitch in the emergency described above and credits Maletz, in 1935, as first clearly recognizing the importance of calcium therapy, though Stanton and Kahn, in 1915, used about a gallon of solution of lime water and calcium chloride for washing the stomach in the successful treatment of a 19 month old girl who had swallowed a roach powder containing about 50 per cent sodium fluoride.

The recommendations of Peters are as follows:

1. Act quickly. Fluoride may kill in a few minutes, and 3 to 4 hours after ingestion is the most frequent reported lethal interval.

2. Start intravenous therapy with glucose in normal saline promptly, both to maintain blood and sugar in case of hepatic glycogen depletion, and to have a venous channel available for transfusion. Shock may kill despite calcium.

3. Wash the stomach gently with saline, or preferably with lime water, and then give lime water at frequent intervals.

4. Have calcium available for intravenous administration and watch closely for signs of tetany. Tetanic death is often rapid.

5. Maintain high urine volume with parenteral fluid.

6. Wash away vomitus, feces and urine promptly to prevent external burns.

The identification of symptons of acute fluoride poisoning and recommendations for treatment given by the Council on Dental Therapeutics in Accepted Dental Remedies are as follows:

Symptoms --- Nausea and vomiting; burning, cramp like abdominal pains; diarrhea. Sometimes tremors or convulsions. Greyish blue cyanosis. Urine and blood show presence of fluoride.

Treatment --- Copious gastric lavage with limewater or 1 per cent calcium chloride solution. Calcium gluconate 1 Gm (10 cc. of 10 per cent) intramuscularly or calcium chloride 1 Gm. (10 cc. of 10 per cent) in water, intravenously. Carbon dioxide-oxygen inhalation, or artificial respiration if necessary. External heat. Intravenous glucose or normal saline if necessary.

Is Use of 2 per cent Sodium Fluoride Solution Hazardous?
In our opinion, the application of 2 per cent sodium fluoride in water solution topically is perfectly safe under the conditions of application in the dental office by the dentist or dental hygienist. It has been estimated that at most 2 cc. of the 2 per cent solution are used in a single application. This volume would contain 20 mg. of fluorine (40 mg. of sodium fluoride), most of which is rinsed from the teeth and ejected from the mouth if the customary practice as described by Knutson is followed. Even if the patient swallowed the entire amount, there would be no physiological effect. The patient would not be nauseated or harmed.

The 2 per cent solution of sodium fluoride should never under any circumstances be placed in the home. The 2 per cent aqueous solution of sodium fluoride is colorless, odorless and has only a salty taste. Ten cubic centimeters of this solution accidentally drunk by a baby would give a dose of 100 mg. of fluorine -- the lethal dose cited by Gettler and Ellerbrook for an adult. If bottles of 2 per cent sodium fluoride solution are permitted in homes, it will only be a matter of time before records of children's deaths will be found in the dental and medical literature. The 2 per cent solution of sodium fluoride is too toxic to be permitted in homes.

Chronic Poisoning: High-Grade

The classical effects of chronic poisoning seen industrially, and in those ingesting drinking water with excessive concentrations of fluorides, are stiffness of the joints, exostoses, moth-eaten bones, calcification of the ligaments and, of special interest to dentists, changes in the roentgenograms of the jaw bone characterized by heavy trabeculae.

Stiff Backs. --- Shortt, Pandit and Raghavachari observed stiffness of the backs of individuals over 30 years of age in districts near Madras, India. It was a common belief that the condition derived from the water supply. Shortt and his colleagues noted severe mottled enamel and found from 0 to 10 ppm. fluorine in the waters. Pandit, Raghavachari, Rao and Krishnamurti estimated on the basis of 6 pints of daily water ingestion, that an intake of 5.4 mg. of fluoride produced a slight incidence of stiff backs; in districts with the most extreme cases the estimates ranged up to 24 mg. They said "bone affections were fairly prevalent" in a town "with a fluoride content of only 2 ppm. in their water supply." Osteosclerosis has been reported associated with mottled enamel by Capizzano, Paterson Toledo, Megy and Valotta; Capizzano, Valotta and Megy, Mascheroni, Munos and Reussi. Ockerse found 8 cases of osteoporosis in South Africa associated with mottled enamel from 12 ppm. fluorine in the water supply. Kemp, Murray and Wilson described two cases with skeletal changes associated with severe mottled enamel. Linsman and McMurray found severe osteosclerosis in a man, age 22, with a history of exposure to 12 ppm. fluorine in water. This case at autopsy showed a cystic condition of one kidney injury and atrophy of the other. There was a history of kidney injury at 15 years. They speculated as to whether the fluorine had aggravated the kidney injury or retention of fluorine had promoted development of osteosclerosis. Lyth described four cases of spondylitis in Chinese associated with mottled enamel and fluorine in the drinking water up to 13 ppm.

Although the mechanism by which high-grade chronic fluorine poisoning develops has not been described, attention should be drawn to the fact that all of the changes are associated with derangements in mineral metabolism. It has been known for some time that fluoride is a powerful poison of the phosphatase essential for calcification. Perhaps this action is responsible for the development of crippling fluorosis.

Daily Fluoride Intake Associated with Chronic High-Grade Fluorosis. --- From analyses of the urinary excretion of fluoride by cryolite workers in Denmark, the opinion has been stated that crippling fluorosis develops in individuals whose intake of fluoride exceeds 20 mg. per day for a period of 10 to 20 years. The fluoride intake of the persons referred to above who developed crippling fluorosis from drinking fluoride-rich waters is unknown, although amounts of the order of 20 mg. or more per day are plausible.

McClure has reviewed the literature on the excretion of fluoride and has concluded that at least 90 per cent of ingested fluoride appears in urine, feces and sweat when the amounts taken are in the ranges proposed for fluoridization of water. Certainly there is fluoride retained by the bones as there is ample evidence that the fluorine content of bones is increased with age. There are available reliable methods for the estimation of urinary fluorides. Consequently, in industries with known fluoride exposures, urinary analyses should prevent the occurrence of this crippling disorder. In the case of individuals drinking water containing excessive amounts of fluoride, analyses of the water supply and of the urine should make possible the control of this hazard.

Is There Danger of Chronic High-Grade Fluorosis? --- The volume of 2 per cent sodium fluoride solution applied in a topical treatment as was stated, might be 2 cc. containing 20 mg. of fluorine. On the basis of the best available opinion, if this entire amount were swallowed and if the treatment were continued daily for ten to twenty years, crippling fluorosis might occur. Such a prospect is so fantastic that no further comment is needed.

The question might be raised as to the accumulation of fluoride. For example, if fruits and vegetables are sprayed with a fluoride insecticide and if they are cooked in a fluoride water (1 ppm.) in which the fluoride content is increased by evaporation of the water, and if the patient is drinking 1 ppm. fluorine water, and taking fluoride vitamin tablets containing ½ mg. of fluorine, and is using a fluoride dentifrice, would all of these sources of fluoride combine to exceed a limit of safety from crippling fluorosis? The answer, in our opinion, is negative. It is almost impossible to imagine any set of circumstances in which the fluoride intake might become sufficient to bring about chronic high-grade fluorosis, if the fluorine content of the water is of the order of 1 ppm.

Chronic Poisoning: Low-Grade

Since mottled enamel was first effectively described by Black and McKay in 1916, this disfiguring hypoplasia has been the object of continued and large-scale epidemiological study. The condition has been graded as to severity by Dean into six classes or, as distinct from "normal": (1) questionable -- a few white flecks in groups of about 25 children; (2) very mild -- small opaque paper white areas scattered irregularly, involving less than 25 per cent of the tooth surface; (3) mild--the areas involve at least half of the tooth surface and a few brown stains may occur; (4) moderate -- all of the tooth surface is involved with no change in tooth form, except minute pitting; brown stain is frequent; (5) moderately severe --a greater depth of the enamel is involved; pitting is more frequent with brown stain, if present, generally deeper in hue. (6) severe -- hypoplasia so marked the form of the teeth is at times affected; pits are deeper and often confluent; stains are brown to chocolate or black.

The histogenesis of mottled enamel has been shown to involve more or less acutely hypoplastic and ultimately cuboidal ameloblasts. With the loss of form of the ameloblasts goes a loss of function so that, in advanced lesions, the ameloblast activity is almost entirely gone. The failure of the ameloblast produces the loss of tooth structure seen in severe mottling. At present, the origin of the stain is not understood. The interrod cement substance may be influenced as well as the formation of the rods themselves. The changes responsibile for the opalescence and for the tiny white spots in the mild grades of mottling are likewise not understood. Since mottled enamel arises from interference with ameloblastic activity, it is obvious that the condition can be produced only during the first eight years of life when teeth are calcifying.

DeEds found in vitro depression of bone phosphatase activity by sodium fluoride in "one two-hundreth molar" concentration. This is of the order of 100 ppm. fluorine.

Daily Fluoride Intake Associated with Mottled Enamel--- H. V. Smith -- concluded from observations in Arizona:

The evidence indicates strongly that any water with a fluorine content of 0.9 ppm. (when analyzed by the Foster, Willard, or Sanchis methods)

or over is dangerous from the standpoint of probable damage to the teeth.

Badger has also reported cases of mottled enamel in children drinking from a community water supply in New Mexico containing 0.9 ppm. fluorine. But Dean, Jay, Arnold, McClure and Elvove reported only 47 per cent of the children of Galesburg, Illinois, "showed some form of mottled enamel generally of a very mild type. The remainder, 129, were classified as normal or questionable." The fluorine concentration of Galesburg water was twice that considered dangerous by Smith and Badger. The probable explanation of these differences lies in the hot, dry climate of Arizona and New Mexico compared to the relatively humid, cooler environment of Galesburg, Illinois. It is therefore, advisable to consider that in the fluoridization of water supplies, in the summer mottled enamel can be caused by fluorine at 1 ppm. whereas in the winter months a higher level may be tolerated.

The conclusions of Smith apparently early dominated the control of fluorides in water supplies as the drinking water standards for the United States were set tentatively at 1.0 ppm. fluorine as a maximum. An editorial referred to 1.0 ppm. as the permissible maximum. The limit for fluorine in water supplies was set at 1.5 ppm. in 1946. Enforcement of this arbitrary limit would call for modification or rejection of the water supply of Galesburg, Illinois.

The relationship between severity of mottling and the fluoride content of communal water supplies has been clearly established by the often quoted investigations of Dean and colleagues. Hodge has found a simple, linear relationship between the logarithm of the fluorine content of a community water supply and (a) the index of mottled enamel and (b) the reduction of dental caries. He has suggested that the point of intersection of the lines "might be called the 'point of minimum caries with minimum mottled enamel' or the 'point of maximum usefulness of fluorides with minimum harm'."

The treatment of mottled enamel as an endemic disease obviously is a problem of prevention. Many cities carried out expensive procedures to lower the fluoride content in the drinking water to nonmottling levels following the demonstration in 1931 by Smith, Lantz and Smith, and independently by Churchill, that fluoride was responsible for this dystrophy. Where fluorine is present in waters at levels to cause mottled enamel two procedures are available: seek other sources of water or remove the fluorides. In either case the level of fluorides should not be reduced below 1 ppm. and it may be found advisable in many localities to leave the amount of fluorine at higher levels for most of winter, spring and fall. Therefore if the source of water is changed it may be advisable to blend the new water with the old to obtain the desired fluorine level.

Nichols has reviewed the methods of treatment of water to reduce the fluorine content. Two general procedures are available, namely, those based on reaction of the fluoride with hydroxyapatite, variously prepared, or with alumina. The latter reagent is of further importance since, if sodium aluminate treatment of water supplies is used, addition of sodium fluoride for caries prevention must be done after the lime flocculation. Otherwise an appreciable amount of the added fluoride will be lost.

To solve the esthetic problem for the victims of mottled enamel, local treatments are sometimes employed (Younger, reference 9, p. 50). However, porcelain facings, jacket crowns or even dentures may be required.

Is There a Danger of Mottled Enamel From Prophylactic Applications of Fluorine? --- When fluorides are added to public water supplies, the total fluoride content is usually set at 1 ppm. or slightly more. This concentration has been indicated as able to confer most of the reduction in dental caries attainable by the use of fluorides. From the charts shown by Hodge, it is clear that, on the average, the mottling in persons drinking such water will be less than the "very mild" category. It should be reiterated that in the community from which such an average figure is obtained, there will be a few persons who develop "very mild" or "mild" mottling. It is our opinion that this mottling will never be disfiguring.

What of the person drinking such water who receives fluoride in a topical application? The extra amount of fluorine ingested on the day of treatment may well be several milligrams but should not exceed 20 mg. Studies of the rate of excretion of fluorides indicate that a single dose of fluorides is rapidly excreted, so that the effects would not be produced after a day or two. Consequently, even a program of three or four applications at weekly intervals once or twice a year would not add enough fluoride to have any recognizable action. On the other hand, it is possible that persons drinking water containing 1 ppm. who also ingest fluoride tablets daily during the first eight years of life, might be able to increase the total fluoride absorbed by the body to the extent of producing disfiguring mottling. The amounts of fluoride that may be absorbed from the use of fluoride-containing dentifrices, mouth washes or chewing gum is not known at present so that these sources cannot be evaluated.

A possible future danger of mottled enamel lies in over-enthusiasm to provide fluorides for the prevention of dental caries. Proposals have been made for the use of bone meal because of its fluorine content, which may range up to 1,000 ppm. Fluoride-containing tablets are being sold. "The food in the diet will contribute on the average of 0.20-0.30 mg. of fluorine daily" but there are foods which have high fluorine content such as canned salmon, including bones, containing up to 6 ppm. and fish pastes with up to 9 ppm. McClure has recently summarized the data of the fluorine content of foods.

Safety of Prophylactic Application of Fluorine ---Hodges, Fareed, Ruggy and Chadnoff examined 86 persons from age 7 1/2 to 71 years in towns with fluorine from 1.2 to 3.0 ppm. in the water. They found no evidence by roentgenography of sclerosis of the skeleton.

Bone Fracture; Growth. --- McClure studied the relation of fluoride from water supplies to the height, weight and bone-fracture experience of 1,458 high school boys and 2,529 young men taking physical examinations at United States armed forces induction centers. The bone fractures were classified as (a) arm, wrist or elbow (b) collar bone (c) leg, knee or ankle (d) nose and (e) other. He concluded;

There was no relation of fracture experience to fluoride exposure. The average height and body weight of all the boys compared favorably with other height-weight data and accepted standards. The height-weight data were not related to fluoride exposures ....

While these data on bone-fracture experience for both men and boys of these ages do not permit final conclusions, they do suggest strongly, that no serious impairment in skeletal performance, as might be manifest in number of broken bones, seems related to exposure to fluoride domestic waters of the concentrations studied in this survey.

Texas men exposed to highest water-fluorine concentrations and Oklahoma men averaged 69.6 and 69.4 inches in height (weight 149.0 and 142.4 pounds), respectively. Men from rural Indiana and Indianapolis averaged 68.1 and 68.3 inches in height, 146.8 and 146.2 pounds in weight respectively, Washington, D.C., men averaged 69.3 inches and weighed 151.2 pounds on the average. New Hampshire men were 67.3 inches tall and weighed 149.6 pounds on the average. These height weight figures showed no relation to fluoride exposure.

Thyroid Metabolism --- Evans and Phillips reviewed the evidence of fluorine as influencing the course of hyperthyroidism. They analyzed thyroids of forty thyroidectomy cases for fluorine and iodine and compared the findings with the basal metabolic rates. They concluded: "The data obtained gave no definite evidence that fluorine in any way played a part in human hyperthyroidism by its action on the thyroid gland."

Effects on Hearing --- There is somepossibility that fluorine of water supplies may have beneficial effects on hearing. Lewy found hearing defects in 4.9 per cent of 109,869 children from low fluorine districts in Illinois, and 2.8 per cent in 20,488 from districts with fluorine not over 1.4 ppm.

Mottled Enamel: A Delicate Sign. --- The appearance of mottled enamel appears to be the most delicate sign of chronic fluorine toxicity. In Table 2, some of the effects of minimum dosages of fluorine have been listed.

From the evidence available at present, a sample of which has been presented in Table 2, it appears that mottled enamel is the most delicate known effect of fluorides. As far as is known, there is no other toxic effect from ingesting amounts of fluoride as small as those taken when the drinking water contains 1 ppm. fluorine.

Table 2 - - - Minimum dosage of fluorine to produce various effects in animals -

Effect	Dosage	Species
Growth retardation	20 mg./kg./day	Rat
Growth retardation	313 ppm.	Rat
Growth retardation	2-3 mg./kg./day	Cat
Reduction in birth weight	190 ppm.	Rat
Milk yield decrease	2-3 mg./kg./day	Cow
Survival to weaning	226 ppm.	Rat
Calcium retention decreased	623 ppm.	Rat
Calcium balance unchanged	CaF_2 4-6 mg./kg./day	Pig
Bleached incisors	14 ppm. (added)	Rat
Striations of incisors	4 ppm. in water	Rat
Mottled enamel	1 ppm. in water	Human

Local Actions

Fluorides applied locally in high concentrations may have deleterious effects of importance to dentistry.

Topical Applications of Fluorides --- Abelson reported a case of dermatitis affecting the first two fingers and thumb of a dentist who had been using sodium fluoride for topical applications for six months. The attacks had occurred at the start of the applications but an attack resulting in blisters had occurred about three weeks prior to Abelson's observation of the case. A patch test with sodium fluoride gave a "late but plus 4 positive reaction."

Considering the small amounts of sodium fluoride actually used in recommended topical application procedures --- about 1 cc. of 2 per cent solution or about 10 mg. of fluorine -- there is no danger of any toxic sequelae. Consequently no precautionary measures are indicated such as a follow-up with calcium chloride solution or other calcium salts as used by Brady.

Possible Pulp Injury in Desensitizing Dentin. --- Barker used Lukomsky's paste in cavities and found it resulted in a large pulp abscess, fibrosis of the pulp, destruction of odontoblasts and thickening of blood vessels. Hoyt and Bibby following Lukomsky, found that when a 33 per cent sodium fluoride paste was used in cavity preparation it caused intense pain on contact with freshly exposed dentin.

Lefkowitz and Bodecker showed that crystals of sodium fluoride placed in artificial cavities in human teeth caused pulp abscesses and hyperemia. They indicated more severe effects in human teeth.

Rovelstad included sodium fluoride in various ways in cavities prepared in children's teeth. These teeth were then extracted, for orthodontic reasons, (a) immediately, (b) 18 hours and (c) one week after application. "All of the teeth to which the drug was applied evidenced some pulpal reaction, with the exception of those removed immediately after the drug application."

Injections of Concentrated Solutions of Sodium Fluoride for Pyorrhea. --- The ease of removal of tightly adherent masses of tartar from extracted teeth by aqueous solutions of hydrofluoric acid led Head to apply a less injurious fluoride solution to the exposed portions of teeth in patients suffering from pyorrhea. He described the preparation of a 23 per cent solution of ammonium bifluoride in water and the beneficial effects when this solution was "injected once or twice a week in pockets around loose teeth." No systemic or local injury was noted although Head warned that "care must be taken not to inject into fresh cuts, as such procedure will cause great pain". No other reports of this use of fluoride solution appeared until Lukomsky recommended a similar use of sodium fluoride.

Summary

1. The possible hazards attendant on the use of fluorides in dentistry have been discussed. The most important applications of fluoride at present are (a) fluoridization of water, (b) topical use of concentrated solutions, and (c) fluoride paste used to desensitize dentin. Other uses of fluoride are cited that

are, at present, not therapeutically important.

2. Two per cent solutions of sodium fluoride as used for topical applications are perfectly safe when the application is made in the dental office. The two per cent solution is too toxic to be kept in homes and should never be prescribed.

3. Chronic, crippling fluorosis will never appear as a result of dental uses of fluorides.

4. Mottled enamel, the most delicate sign of fluoride toxicity, will be found when fluoridization is carried out at about 1 ppm. of fluoride only in a very few individuals in whom very mild mottling will occur. No unesthetic marring of the teeth should occur.

5. Persons drinking communal water supplies containing about 1 ppm. fluorine conceivably might increase the fluoride intake by daily accessory fluoride administration to a level sufficient to cause mottled enamel.

6. There is no other known toxic effect of drinking water containing 1 ppm. fluorine than the "very mild" mottling of the teeth.

7. Repeated local applications of fluorides on soft tissues, for example, the skin of the fingers, has produced dermatitis in a single recorded case.

8. Concentrated preparations of sodium fluoride have been shown to produce pulpal reactions when applied to freshly cut dentin for desensitization.

TOXICOLOGICAL EVIDENCE FOR THE SAFETY OF THE FLUORIDATION OF PUBLIC WATER SUPPLIES*

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The extravagance of the variously motivated statements frequently heard in opposition to fluoridation wherever it is under consideration may lead officials who must explain this prophylactic measure to the public to discount the fact that many citizens still remain unconvinced of the safety of this procedure, despite the assurances of medical, dental, and public health authorities. Many are aware that a few scientists, physicians, and dentists, some of whom have contributed to our knowledge of the physiological effects of fluorides, have testified before a Congressional committee that, while not condemning fluoridation, they nevertheless hesitate to recommend its adoption at present. Unless public health authorities inform the public of the evidence upon which they base their belief in its safety, many persons will accept statements that little is known of the toxicity of fluorides and that the epidemiological evidence relied upon by the advocates of fluoridation fails to reveal adequately any adverse effects that may be associated with individual variations in susceptibility. For those who must present the subject a discussion of the present status of our knowledge of the toxicology of the fluoride ion may be helpful.

ACUTE TOXICITY

It is well known that inorganic fluorides are highly toxic, and that their use in the household as roach poisons has led to the poisoning of numbers of people into whose food they have been introduced accidentally. The study of acute poisoning has pertinence only in so far as it may reveal which organs are most vulnerable to the action of fluorides. The pathalogic picture is one of hemorrhagic gastroenteritis and acute toxic nephritis, accompanied by more or less damage to the liver and other organs. Some of the signs and symptoms have been ascribed to a lowering of the blood calcium, but others result from the inhibitory action of the fluoride ion upon the activity of one or more enzymes that function in the sequence of reactions by which the energy of carbohydrates is made available for the metabolic activity of the tissues. The dose that is lethal when ingested by rabbits has been variously reported as ranging from 50 to 200 mg. of fluoride ion per kilogram of body weight. In human self-experimentation, as much as 250 mg. of sodium fluoride has been taken at one time without harm. It is evident that there need be no fear of the occurrence of acute poisoning as a result of the accidental or deliberate over-fluoridation of a water supply. Any toxic hazard that may be associated with fluoridation could be only that of the cumulative action of small amounts taken daily over a long period of time.

* Presented at a Joint Session of the American School Health Association, the Conference for Health Council Work, and the Dental Health, Public Health Education, and Public Health Nursing Sections of the American Public Health Association at the Eightieth Annual Meeting in Cleveland, Ohio, October 23, 1952.

CHRONIC TOXICITY

Chronic fluorosis was first described as occurring among animals. Darmous, an abnormality of the teeth and bones, occurs among sheep and cattle pastured in North Africa on land where the vegetation is contaminated by fluoride-bearing dusts derived from phosphate deposits. In Iceland, sheep grazing on pastures contaminated with fluoride-containing volcanic ash suffer from Gaddur, a condition in which the teeth are spotted, the bones are thickened, and the animals become lame and weak. Severe cases among sheep, goats, and cattle have occurred both in Europe and in the United States in the vicinity of factories that emit fluoride-containing compounds into the atmosphere. Such cattle have a stiff-legged gait, swollen hock-joints and palpable lumps on their bones as well as irregularly worn teeth.

Many experiments have been performed in the effort to reproduce the condition by incorporating fluorides in the food of rats, dogs, and other animals. Sheep, swine, and cattle, as well as chickens, have also been given fluoride-containing food in order to learn whether phosphate rock, which may contain from 3 to 4 per cent of fluoride, can be used safely as a mineral supplement in the feeding of livestock. Time is not available for a detailed discussion of these investigations, which have been reviewed by Roholm, McClure, Greenwood and DeEds. The continued daily ingestion by rats of diets containing from 7 to 12 ppm. induces signs of dental fluorosis, detectable only by means of a lens. When the diet contains somewhat greater amounts, the incisors become chalky, pitted, and corroded, and changes in the ossious system may result. Dietary levels of from 100 to 230 ppm inhibit growth. Rats that consume diets with 900 or more ppm die after a few weeks. Roholm, who expressed the intake in relation to body weight, concluded that incipient dental fluorosis may be induced by a daily intake of 1 mg. per kg. Five times that intake gave rise to incipient changes in the bones and kidneys, and one of from 10 to 15 mg. per kg. brought about recognizable signs of ill-health. Severe degenerative changes in the organs appeared when the daily intake was from 20 to 25 mg. per kg., and death occurred within a few days or weeks when it was 50 to 100 mg. per kg.

In our laboratory, Largent gave 65 mg. of fluorine daily to each of two 11-months-old littermate dogs, the third littermate serving only as control. It was given to one as sodium fluoride and to the other as cryolite, sodium aluminum fluoride. During the second month the dog given sodium fluoride lost appetite and vomited occasionally , but this did not persist. The administration of fluorides was continued for five years and five months, when it was stopped upon the death of the dog that had been given none. During life, no osseous changes could be detected roentgenographically. The ash of the bones of the dog given sodium fluoride contained 10 times the amount of fluoride found in the case of the dog used as control. Among the soft tissues, increased amounts were found only in the lungs and kidneys, which had 1.77 and 3.01 mg. per kg., respectively. No noteworthy histopathologic changes were found in the organs, and the bones, although chalky in appearance, exhibited no very striking abnormalities. The daily fluoride intake of these two dogs was of the order of 3 to 5 mg. per kg. In an experiment performed over 60 years ago, Brandl and Tappeiner gave as much as 10 mg. per kg. per day to a dog over the period of many months. Of the total of 402.9 grams of sodium fluoride given their dog, 330.5 gm. were recovered from the urine, and 64.6 gm. were found in the tissues, most of it in the bones.

Histological changes have occurred in the tissues of animals of several species following a daily intake great enough to retard growth. In Roholm's experiments, the daily ingestion of 5 to 8 mg. per kg., by dogs has given rise to hematuria and albuminuria, with a histologic picture of degeneration of the epithelium of the kidney tubules, associated with interstitial contracting nephritis. Damage to the liver has been observed in some experiments, although less frequently. An intake of the order of 70 mg. per kg. is required in order to damage the gastric and duodenal mucosa.

Although diminished fertility has been reported in several experiments in which fluorides were fed to rats at a high dietary level, its occurrence may be regarded as secondary to the resulting poor growth or inanition, since rats behaved similarly, when limited to the amounts of a normal diet consumed voluntarily by those fed on fluoride-containing diets. Dietary levels near the threshold for the inhibition of growth did not affect the estrus cycle, although this ceased almost completely when the daily intake of fluoride was 25 mg. per kg.

Anemia has developed in severely poisoned dogs and a gel-like atrophy of the bone marrow has been induced in guinea pigs.

Although, in acute poisoning, the blood calcium may be lowered by about 50 per cent, it is decreased but slightly, if at all, in chronic poisoning, Retention by the bones of growing rats occurs normally unless the dietary content of fluoride is more than three or four hundred parts per million.

It may be concluded from the results of animal experimentation that interference with growth cannot be induced by a daily intake too small to give rise to dental abnormalities and that only after the bones have stored considerable quantities of fluoride does any impairment of skeletal function occur. Estimates by various investigators of the maximum daily intake in milligrams per kilogram of body weight that may be tolerated by animals of various species fall within the following ranges: dairy cattle, 1 to 3; swine, 5 to 12; rats, 10 to 20; guinea pigs, 12 to 20; chickens, 35 to 70. Such variations in susceptibility between species would make hazardous any attempt to predict the maximum safe human intake were there no observations upon the conditions as it occurs in man.

HUMAN FLUOROSIS FROM INDUSTRIAL EXPOSURE

Fluorosis is known to occur among workmen who inhale excessive amount of fluorides as dusts or vapors. In the course of the radiographic chest examinations of 78 Danish miners of cryolite, Moller and Gudjonsson found that 30 exhibited an abnormally increased density of the shadows of the spinal column, pelvis, and ribs. Some men complained of stiffness and pain in their joints, and in some cases the motility of the spine and thorax was reduced. In one man, ankylotic changes had occurred to a degree that caused severe functional impairment. Post-mortem examinations of two who died of intercurrent disease revealed bones that were abnormally heavy and dense, chalky-white and marred by extensive periosteal deposits. The bones of these two persons contained many times the amounts of fluoride, 1 to 6 gm., normally present in human skeletons. The bones of one of them yielded 50 and those of the other 90 gm. of fluoride. The latter quantity had been deposited over a total of 7,500 working days, or an average rate of about 12 mg. per day. It was estimated that the amounts inhaled daily by these two men may have been of the order of 0.2 to 0.35 mg. per kg. of body weight. In neither case did the

organs show any histopathologic changes attributable to fluorides. There were, however among the group as a whole many complaints of digestive disturbances and many of the workers were underweight and anemic.

Industrial fluorosis has occured also in Germany and England, but only a very few cases have been reported in the United States. One was a 58-year old man who had long handled sodium fluoride and whose only complaints were of headache and fatigue. Another was discovered in a man with luetic aortitis who for 18 years had been exposed in a fertilizer factory to rock phosphate. On careful examination, a slight limitation of the motion of his lower spine could be detected, but he had no arthritic pains and no digestive disturbances. He was not anemic and his blood contained normal amounts of calcium and phosphorus.

HUMAN EXPERIMENTATION

In order to learn the rates at which storage in human bones occurs when known amount of fluorides are ingested daily, painstaking investigations in which six persons served as experimental subjects have been in progress for 12 years in our laboratory. By analyzing duplicate amounts of all the food and liquids ingested daily by them over prolonged periods, the average daily intake of fluoride of each subject has been measured. Two of these subjects were found to have ingested 0.49 and 0.72 mg. of fluorine per day, respectively. Within the limits of the accuracy of the sampling and the analyses of food materials and excreta, these persons appeared to be in metabolic balance with respect to fluoride. Subsequently, one of them ingested 6 mg. of extradietary fluoride (sodium salt) per day over a period, this amount being equivalent to 0.095 mg. per kg. of body weight. The amount absorbed into his tissues was determined by deducting from the measured intake the amount eliminated in his feces. An estimate of the amount retained in his body was obtained by deducting the amount excreted in the urine from the amount absorbed. This estimate was in error to the extent that fluoride may have been eliminated through the skin, which could not be measured in an experiment of long duration. When extradietary fluoride was taken as the soluble sodium salt, or when the less soluble calcium salt, was given in solution, 95 per cent of it was absorbed, but when it was given as a poorly soluble solid it was much less readily available, only 77 per cent of that given as cryolite or 37 per cent of that given as bone meal being absorbed. From brief balance experiments in which an attempt was made to measure the elimination through the skin, McClure concluded that when the daily intake did not exceed 4 or 5 mg., the major portion was eliminated from the body. That significant storage must have occurred during a period of 183 days on each of which 6 mg. was taken, however, was shown by the fact that for 11 weeks after this person ceased to take any extradietary fluoride, he continued to excrete considerably greater amounts than he ingested in his diet.

More recently, two persons have taken daily over long periods doses of the sodium salt that provided 3 and 12 mg. of fluoride, respectively, equivalent to 0.05 and to 0.14 mg. per kg. These dosages are well below those that Roholm believed capable of causing skeletal fluorosis. In neither of these persons have radiographic changes occurred in the density of the bones, although one of them took more than 20 gm. of sodium fluoride over a period of 120 weeks. Shortly after they began to take these amounts their urinary fluoride concentrations were 2 and 7 mg. per liter, respectively, but these tended to increase as the experiment progressed. At the start, the retention by the subject who took the lower dosage was 33.7 per cent, but between the 36th and 43rd weeks, it had decreased to 13.9 per cent. A similar trend toward decreasing rates of storage has been observed by others in the case of rats fed diets with either 4 or 12.5 ppm over 225 days.

HUMAN FLUOROSIS FROM WATER-BORNE FLUORIDES

From analyses of the water supplies of many communities in the United States, it has been estimated that over two million people use water with from 0.9 to 2.0 ppm and that three million use water with from 0.9 to 5.1 ppm. In a few areas even greater amounts are present. The chemical source of this naturally occurring fluoride is not known, but it is commonly assumed to be calcium fluoride. Our metabolic data have shown that when calcium fluoride is taken in solution the fluoride ion derived from it behaves as does that from sodium fluoride.

The daily intake of water varies widely with climatic conditions and with the individual, his age and activity. Normally active adults in temperate climate may drink from 1 to 3 liters, but those engaged in labor under desert conditions may require so much as 9 to 10 liters or even more. From many analyses of duplicates of the food and fluids consumed by a 63-year old man and his 57-year old wife, long-time residents of Bartlett, Tex., where the water contained 8 ppm, their average daily intake of fluoride was found to be 15.3 mg., only about 15 per cent of which appeared to be stored. Neither exhibited osseous changes. Their average urinary concentrations were 9.8 and 7.7 mg. per liter, respectively, values very closely approximating the concentration in the drinking water. These observations extend to higher concentrations and to greater ages, the earlier finding of McClure that the average urinary concentrations of groups of young men approximate closely those in the water they drank over the range of 0.2 to 4.7 ppm.

Chronic dental fluorosis occurs almost universally where the water contains 4 or more ppm, and very mild, difficultly detectable alterations in the enamel may be found in about 10 per cent of the children using water with 1 ppm. Belief in the inability of water having the latter concentration to induce the extra dental manifestations of fluorosis depends in part upon the extent to which these may be found when sought for among people using water containing greater amounts. Hodges found no evidence of skeletal fluorosis in x-rays of 31 persons who had lived for 18 to 68 years at Bureau, Ill., where the water has 2.5 ppm., or in those of 86 persons at Kempton, Ill., where the content has varied between 1.3 and 3 ppm. A radiologic survey of 114 persons who had lived for at least 15 years at Bartlett, Tex., where 8 ppm were present, revealed minimal evidence of an increase in the density of the bones of 12 per cent of those examined, but in no case was there any deformity or interference with function. Medical examinations, which included urinalyses and blood counts, revealed no evidence that the residents of Bartlett were less healthy than were those of nearby Cameron where the water contained only 0.3 ppm. Examination of 1,400 high school boys and 1,700 draftees, grouped in accordance with their residence in areas where the water contained 0, 0.1, 0.5, 1.2 or 1.8 ppm., revealed no statistically significant differences in their heights and weights or in the numbers of fractures of bones suffered by them. In the Newburgh experiment on fluoridation as a preventive of dental caries, careful pediatric examinations have revealed no skeletal or other calcium and phosphorus metabolism of two girls with mottled enamel was found normal in balance experiments.

Reports of the endemic occurrence of skeletal fluorosis have, however, come from regions in other parts of the world where the water contains excessive amounts of fluoride, and where, as in India and China, malnutrition is prevalent. Only a few of these are complete enough to be of use in establishing the threshold concentration at which harm may occur. Six natives of South

Africa, who for 19 years had used water containing 11.8 ppm, exhibited characteristic radiographic changes and stiffness of the spine. In China, a few cases have occurred in persons who had used water containing 5.9, 6.3 or 13.1 ppm. No cases are known in which skeletal changes have occurred in regions where there is no mottling of the teeth.

More reliable quantitative information may be obtained by studying the condition as it arises from industrial exposure. Industrial hygienists determine the mean values and the ranges of the concentrations in which a noxious agent may appear in the urine among groups of workers exposed to various degrees of atmospheric concentration, and, by correlating the data with the presence or absence of illness among the various groups, learn which degrees of exposure are harmful and which are safe. The previously mentioned corresponcence between the concentrations of fluorides in the urine and drinking water found among residents of various communities makes it possible to apply this method to data from industrial workers in an appraisal of the safety of fluoridation.

Healthy Danish workmen have urinary fluoride concentrations ranging from 0.3 to 1.6 mg. per liter, with a mean of 0.92 mg. per liter. In the group of cryolite workers which included many with skeletal fluorosis, the mean was 16 and the range 2.4 to 43.4 mg. per liter. In two factories in the United States, increases in the radiographic density of the bones have appeared in men, whose urine was known to have contained 10 or more mg. per liter. More recent data offer some indications that such changes may occur to a slight degree in a few men with urinary concentrations of but 6 mg. per liter.

Like other biological functions, the ability to excrete or to store fluorides may be expected to vary from individual to individual. The instances of early fluorosis of the bones seen among these workers and among a small proportion of the population of Bartlett suggest the threshold concentrations which may affect those persons who may be most prone to store fluoride.

It has been found that the ability of rabbits to excrete administered fluoride is diminished temporarily during the acute state of nephritis induced by giving nephrotoxic agent such as uranium.

The only case in which skeletal fluorosis in the United States has been attributed to water-bone fluoride was discovered incidentally during the illness of a 22-year old man who died of uremia seven years after he had suffered an accidental kidney injury. At necropsy, his right kidney was found to be but a thin-walled, cystic, fluid-filled mass, while the left was small and contracted. During the first seven years of his life he had used water containing 12 ppm. Later, he moved about living, with the exception of two years, in areas where the water contained 4.4 or 5.7 ppm. A somewhat similar case has been reported from South America.

In order to learn something of the rates at which fluoride may be stored by persons with kidney disease, it is suggested that a search be made for evidence of skeletal fluorosis in such x-rays as may be found in the case records of patients with chronic nephritis in hospitals in communities where the water contains known amounts of fluorides. In the unlikely event that evidence of the occurence of fluorosis should be found in patients with chronic nephritis who have used water with no more than 1 ppm, it should be possible for physicians who discover such disease to advise their patients to use nonfluoridated water, which could readily be made available for their use. No evidence exists that water-borne fluoride has been a cause of nephritis. In examinations of many

specimens of the urine of young men who used water with from 2.0 to 5.0 ppm McClure found no more instances of the presence of blood or of albumin than were encountered among those using water with no more than 0.3 ppm. Examination of the mortality rates from nephritis, or other diseases, including cancer, recorded in various communities has revealed no association with the fluoride content of their water supplies.

CONCLUSIONS

The results of animal experimentation show that the prolonged intake of quantities of fluoride too small to induce dental fluorosis does not give rise to any of the nondental manifestations of chronic intoxication by fluorides. Epidemiologic data and clinical and radiographic examination of exposed industrial workers indicate that only when the fluoride content of a water supply exceeds 5 or 6 ppm will its prolonged usage give rise to detectable osseous changes and then only in the most susceptible persons. The evidence as a whole is consistent in offering assurance that bringing the fluoride concentration in communal water supplies to that known to be optimal for dental health is a prophylactic public health procedure which has an ample margin of safety.

REVIEW OF THE BARTLETT-CAMERON SURVEY: A TEN YEAR FLUORIDE STUDY

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REVIEW OF THE BARTLETT-CAMERON SURVEY: A TEN YEAR FLUORIDE STUDY

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Long-standing and widespread interest in the effects of fluoride has stimulated a great number of investigators to study fluorides under varying circumstances. The Public Health Service has been one of these investigator groups. It has been particularly interested in the physiological effects of fluoride in water.

The Bartlett-Cameron study reported here combined the methods of clinical, laboratory, and epidemiological research to further knowledge regarding fluorides. It was begun in 1943 by H. Trendley Dean and Francis A. Arnold, Jr., of the Public Health Service, in the towns of Bartlett and Cameron, Texas. Ten years later the same procedures, with a few additions, were repeated by another Public Health Service team. The purpose was to study a population group which had ingested water containing excessive amounts of naturally occurring fluoride over a long period.[1]

Bartlett was selected because the natural fluoride level of the local water supply was one of the highest in the nation -- 8 ppm fluoride (F) - which is eight times the amount recommended for dental caries prevention. A town with a water supply naturally containing excessive fluoride was selected on the assumption that any association between exposure and physiology might be manifest at a high concentration, particularly after prolonged ingestion. Cameron, comparable in size, location and other characteristics was the control town. Its water supply contained 0.4 ppm of fluoride (F).

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1. Leone, Nicholas C. Medical aspects of excessive fluoride in a water supply: a ten year study. In Fluoridation as a public health measure, Shaw, J.H., editor. Washington, D.C., American Association for the Advancement of Science, 1954.

Bartlett and Cameron are geographically located on a triangle with Temple, Texas, 135 miles due south of Dallas. Bartlett is 20 miles south of Temple, and Cameron 38 miles southeast of Temple. The two towns are about 25 linear miles apart, but are not connected by a direct road. In 1940 the populations of Bartlett and Cameron were 1,668 and 5,040 and in 1953, 1,706 and 5,272 respectively.

In March 1952 an experimental defluoridation unit was put into operation in Bartlett in an attempt to reduce the fluoride content of the water to 1.0 ppm fluoride (F), a level that provided dental caries protection without producing mottled enamel. Since the installation of the unit, the fluoride content of the water has varied considerably because of necessary mechanical and experimental changes. However, it has remained somewhat above the desired level of 1.0 ppm fluoride (F). By 1953 the Bartlett subjects in the study had ingested fluorides at high levels for many years. Any significant pathological manifestations of prolonged exposure would not be expected to have regressed materially in the 18 months of partial defluoridation.

The 237 individuals who were studied were about evenly divided between the two towns. They were persons who had lived in their respective communities for a minimum of 15 years prior to 1943. The average length of residence, at the end of the study period, was 37 years for the Bartlett group and 38 years for those in Cameron. The subjects' ages ranged from 15 to 68 years at the beginning of the study. All were of the white race.

Procedure

In 1943 a medical-dental team from the Public Health Service examined 116 subjects in Bartlett and 121 in Cameron.

The 1943 group was selected after a preliminary survey that covered approximately every household in Bartlett and every third household in Cameron. An adult member of each household was interviewed and history forms were made out for each household member. On the basis of the data so obtained, a random sample was chosen from those who met the basic requirement - 15 years or more of continuous residence prior to 1943.

Ten years later, in 1953, all of the original subjects were accounted for, and all but 10 of the living were re-examined. Approximately 71 per cent of the 237 subjects in the 1943 survey still resided in Bartlett and Cameron. Information on the deceased, another 8 per cent, was obtained from the next of kin, and copies of the death certificates were obtained to establish cause of death. Because of the unusual success in accounting for 79 per cent of the subjects locally, it was deemed practicable to follow up the remaining 21 per cent who had moved from the study areas. As a result, all of the 1943 subjects, living, deceased or "removed" were accounted for in the 1953 study.

Forty-seven subjects had moved away from the two towns in the ten years; two had moved to California, one to Oklahoma, and one to New York City. Forty-three of the "removed" subjects still lived in Texas. Of these, 37 were examined and the data were obtained by the same procedures as used for those who remained in residence.

The ten living persons who were not examined were interviewed by

personal contact, telephone or mail, and a ten year medical and residence history was obtained. None reported acute, chronic, serious or debilitating illnesses.

The data were evaluated for the group as a whole and separately for those who remained in residence. Analysis of the findings for the subjects who remained in continuous residence and for the whole group, including the "removed," showed no important differences; to assure comparability, however, the present report deals only with the resident group.

The 1943 and 1953 procedures were essentially parallel. They included a medical history, physical and dental examination, roentgenograms, blood and urine studies. In the earlier study the physical and dental examinations and the laboratory work were done locally in the respective towns, and the patients were later transported to the Scott and White Clinic in Temple, Texas, for their roentgenographic examination.

The 1953 procedure differed slightly in that the majority of physical and laboratory examinations, as well as the roentgenographic, were done at the Scott and White Clinic by Public Health Service personnel. Blood and urine analyses were done by the Scott and White Clinic technicians, and the chief of radiology (Dr. Clyde Stevenson) supervised the taking of roentgenograms and made the initial roentgenographic interpretations in 1943 and 1953. Both sets of films were later evaluated by Dr. Merrill Sosman, chief of the radilogy department, Peter Bent Brigham Hospital, Boston, and consultant to the National Institute of Dental Research, and Dr. Theodore Hilbish, chief of the department of diagnostic x-ray in the Clinical Center, National Institutes of Health.

Physical Examination - A complete physical examination was given all subjects in 1943 and in 1953. The laboratory studies included a determination of hemoglobin, red and white blood cell counts, a differential white count, and a serologic test for syphilis. Urine determinations included specific gravity, qualitative albumin and sugar, and microscopic examination.

In 1953, a few additional procedures were included. Rectal and pelvic examinations were made of most of the women, and prostate examinations were routine in men. Hematocrit, sedimentation rate, and blood calcium were determined. When indicated, further studies were made, such as acid and alkaline phosphatase, blood sugar, and special hematology. Consultant service was used when indicated.

The removed subjects were given essentially the same examination by the same Public Health Service physician.

Roentgenographic Examination - The roentgenograms taken at the Scott and White Clinic were made on a 500 ma roentgenographic unit with a rotating anode tube. Emphasis was placed on bone detail. Anteroposterior views of the dorsal spine, the lumbar spine , and the pelvis with the proximal third of the femur were taken for each subject. When a question of unusual findings arose, a roentgenographic bone survey was made that consisted of the following views: lateral skull, cervical spine, left upper arm, forearm and hand, and right femur, lower leg and foot.

Similar roentgenograms were taken at the nearest available facility for the removed subjects.

Oral Examinations - All of the physical examinations included an oral examination by the Public Health Service team. The majority of the participants seen at the Scott and White Clinic in 1953 were also given a complete dental examination by a Public Health Service dentist, and complete dental roentgenograms were taken of practically all of the subjects, including the edentulous. Estimations were made on the degree and prevalence of dental fluorosis, dental caries experience, gingivitis, alveolar bone loss, and other types of oral pathology. The details of the dental findings are reported on page 272 of this issue of The Journal in an article by Dr. Zimmermann.

It should be noted that this investigation was not initially designed as a dental caries-fluoride study. The oral findings constitute but one phase of a medical-experience study. The age distribution of the participants was predominantly in the older age groups and, therefore, not as suitable as might be desired for some types of dental studies.

Observations

Analysis of the data produced the following conclusions:

1. As was expected, dental fluorosis was significantly greater in Bartlett than in Cameron (all of the participants born and in continuous residence in Bartlett during the tooth formative period exhibited positive evidence of dental fluorosis).

(a) The two groups showed no significant differences in the ten year period with respect to changes in blood pressure, arthritic conditions, eyes, thyroid disorders, hearing, tumors, cysts, bones and bone fractures, and the urinary system.

(b) The incidence of cardiovascular disease was higher in the area containing 0.4 ppm of fluoride, an observation unrelated to fluoride ingestion.

(c) There were no significant differences between the age-adjusted death rates in the two towns.

(d) The only difference in laboratory findings was in the white blood cell count, which tended to be higher in the fluoride area in 1953. White blood cell counts are normally subject to considerable variation and, when viewed in the light of clinical experience, this finding does not suggest an association with fluoride intake.

When the data are reviewed critically, it is clear that the medical characteristics of the two groups, with the exception of dental fluorosis, do not differ more than would be expected of two comparable towns with or without an excess of fluoride in the water supply

Table 1. Incidence of abnormal clinical findings, 1943-1953. (Participants residing in study area for the ten-year period)

Characteristic studied	Bartlett			Cameron			Significant difference (P=0.05)
	No. at risk	No. abnormal	Rate (per cent)	No. at risk	No. abnormal	Rate (per cent)	
Arthritic change	80	11	13.8	89	13	14.6	No
Blood Pressure sys. 151 mm/Hg and over	58	18	31.0	81	20	24.7	No
Dias. 100 mm/ Hg & over	73	11	15.1	83	11	13.3	No
Pulse pressure 75mm/Hg & over	70	9	12.9	89	16	18.0	No
Bone changes*							
Density+	74	7	9.5	81	2	2.5	No
Course trabeculation	74	4	5.4	81	2	2.5	No
Hypertrophic	74	8	10.8	81	6	7.4	No
Spurs	74	1	1.4	81	4	4.9	No
Osteoporosis	74	5	6.8	81	10	12.3	No
Bone, increased density (new cases)	66	1	1.5	79	--	-- -	--
Cataract and/or lens opacity	79	8	10.1	85	12	14.1	No
Thyroid	74	3	4.1	82	6	7.3	No
Cardiovascular (except uncomplicated hypertension)	80	10	12.5	92	22	23.9	Yes
Hearing (decreased acuity)	72	14	19.4	78	10	12.8	No
Tumor and/or cysts	80	12	15.0	92	10	10.9	No
Fractures	80	12	15.0	92	7	7.6	No
Urinary tract calculi	72	14	19.4	76	12	15.8	No
Gall stones	73	0	0.0	80	1	1.2	No

*Bone changes determined by simultaneous reading of identical views of roentgenograms taken in 1943 and repeated in 1953.

+Bartlett: 4 increased density, 3 decreased density. Cameron: 2 increased density.

Table 2 - Prevalence of abnormal laboratory findings, 1943 and 1953. (Participants residing in study area for the ten-year period)

Laboratory determination	Year	Bartlett			Cameron			Significant difference (P=0.05)
		No. examined	No. abnormal	Rate (per cent)	No. examined	No. abnormal	Rate (per cent)	
Hemoglobin	1943	116	34	29.3	121	37	30.6	No
	1953	79	20	25.3	83	26	31.3	No
Hematocrit	1943	---	--	----	---	--	----	--
	1953	79	5	6.3	82	7	8.5	No
Red blood count	1943	116	25	21.6	121	24	19.8	No
	1953	80	6	7.5	85	2	2.4	No
White blood count	1943	116	17	14.7	121	5	4.1	Yes
	1953	78	11	14.1	82	7	8.5	No
Differential count Neutrophils	1943	71	15	21.1	71	6	8.5	Yes
	1953	78	23	29.5	82	13	15.9	Yes
Lymphocytes	1943	71	2	2.8	71	1	1.4	No
	1953	78	35	44.9	82	36	43.9	No
Eosinophils	1943	71	0	0.0	71	0	0.0	No
	1953	78	6	7.7	82	14	17.1	No
Sedimentation rate	1943	---	--	----	---	--	----	--
	1953	79	31	39.2	83	22	26.5	No
Blood calcium	1943	---	--	----	---	--	----	--
	1953	79	9	11.4	66	7	10.6	No
Serology (S.T.S.)	1943	71	2	2.8	71	3	4.2	No
	1953	84	2	2.4	95	2	2.1	No
Urine albumin	1943	115	3	2.6	121	10	8.3	Yes
	1953	77	5	6.5	85	12	14.1	No
Urine glucose	1943	115	2	1.7	121	4	3.3	No
	1953	77	0	0.0	85	1	1.2	No

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